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# NEUROLOGICAL
AND
# OTHER PAPERS

REPRINTED FROM THE WRITINGS OF

JOHN MICHELL CLARKE,
*M.A., M.D. Cantab., LL.D. Bristol, F.R.C.P.,*
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# PREFATORY NOTE

At a meeting of the Honorary Staffs of the Bristol Royal Infirmary and the Bristol General Hospital, held in the University of Bristol on June 28th, 1918, it was resolved to collect funds for establishing a memorial of the life and work of the late Dr. J. Michell Clarke, Pro-Vice-Chancellor and joint Professor of Medicine in the University of Bristol, and Senior Physician to the Bristol General Hospital. The endowment of the Bristol Medical Library was further suggested as a suitable form for such a memorial. Dr. Michell Clarke's energies had been largely devoted to the cause of medical education and research, and it was thought that at least a part of his aims in this direction would be substantially advanced by providing permanently for the supply of books and periodicals dealing with clinical medicine for the use of medical practitioners and the students in the Medical School.

An Appeal Committee, representative of British medical education in general, of the civic and University authorities, of the local medical profession, of the bodies responsible for the management of the Medical Library, and of the personal friends of Dr. Michell Clarke, was therefore brought together, and as a result of their labours the sum of £1,154 was collected. The greater part of this was invested and placed in the hands of Trustees, the income therefrom to be expended in the manner already indicated.

It was, however, suggested to the Executive Committee that the memorial should include the publication in book form of some of Dr. Michell Clarke's more important contributions to medical and scientific literature. This suggestion was duly brought to the notice of the Appeal Committee, who after careful and sympathetic consideration came to the conclusion that such a volume would be not only of interest to Dr. Michell Clarke's many personal friends, but also of value to the profession at large. Possibly had his life been prolonged beyond the strenuous and exacting period of the war he would himself have recorded a larger portion of his valuable researches and wide experience in books which would have been at once complete and easily accessible; as it is, most of his work remains in periodical publications, scattered over a considerable number of years and in a variety of Medical Journals. It seemed, therefore, by no means unfitting that the memorial to him should include some such collection as is now offered to the profession.

The two members of the Executive Committee to whom the task of preparing this volume was delegated by their colleagues have endeavoured to make it representative of the best of Dr. Michell Clarke's work; the papers, each of which has been reprinted in its entirety, have been selected from the large amount of material at their disposal, so as to include, first of all, the more important contributions to the science of Neurology, in which their late colleague was a well-recognised authority and original worker; secondly, they have inserted several valuable papers on other subjects illustrating Dr. Michell Clarke's comprehensive interest in general medicine; and lastly, by reprinting here the address given in 1905, they intend to show his wide and scholarly outlook and high level of humanistic culture.

Their grateful acknowledgments are due to the Editors of the various Journals in which these papers originally appeared for the permission given to reprint them, and for the loan in some cases of the illustrations which accompanied them. A list of these appears in the Table of Contents.

In concluding their work, they desire to point out that their task, though an interesting and honourable one, has not been easy ; others, no doubt, might have made a different selection or proceeded on other lines. They are, however, confident that the high excellence of all that Dr. Michell Clarke wrote renders almost any selection of permanent interest, and no unfitting memorial to a man whom all who knew him delighted to honour.

J. M. Fortescue-Brickdale.
G. Parker.

# BIOGRAPHICAL MEMOIR

(Reprinted from the *Bristol Medico-Chirurgical Journal*, vol. xxxvi., No. 135.)

John Michell Clarke was born at Clifton in 1859, and was sent first to a preparatory school, and then to Dr. Hudson's, of Manilla Hall, one of the famous private schools which flourished here at that time. When he was sixteen he passed into the new and stately buildings of Clifton College, which had recently commenced its prosperous career. Here for three years as a South Town boy he worked his way to the Sixth Form, and left to enter at Gonville and Caius College, Cambridge.

The medical school there had recently been reorganised under Sir George M. Humphry, one of the most inspiring teachers of the age, who gathered around him such brilliant men as Michael Foster, Gaskell, and Balfour in a determined effort to make that school the most progressive and scientific in England. Clarke soon absorbed the enthusiasm and spirit of his surroundings, but after taking his degree in the Natural Sciences Tripos of 1882 and holding a Demonstratorship of Anatomy he had to leave for clinical study elsewhere.

He dressed for Mr. Nelson Dobson at the Bristol General Hospital, but had the misfortune to get diphtheria in an attempt to revive a drowning man. For a long while he was ill with cardiac complications, but eventually regained vigorous health and went up to St. Thomas's Hospital, where he made the most of his opportunities of studying medicine under such teachers as Ord, Bristowe and Buzzard. He was holding office as House Physician when the sudden death of his father in 1885 and the need of taking his place in Clifton forced him to give up his appointment and the possibility of practice in London.

Settling down in Clifton, he was elected Assistant Physician and Pathologist at the Bristol General Hospital in 1886, and from that time to the day of his death nothing ever lessened the devotion with which he worked for that hospital and his patients there. He was made full Physician in 1893, and for thirty years he took an active share in all the improvements made during that period. In his earlier days he did most of the pathological and museum duties himself, but later on the Committee put up a fine range of buildings and appointed a whole time Pathologist in response to the representations of Clarke and his colleagues. In this as in every other matter his time and careful thought were ungrudgingly given both to the Committee and the Staff, by all of whom his sterling qualities were most warmly appreciated. At this time a movement was going on in the country for the better training of nurses and the improvement of their status. Michell Clarke gave himself warmly to support the efforts of the Hospital Committee, and changes were worked out which revolutionised the education of nurses there, enabling them to make some provision for the future, and created a highly-trained staff, who were available both for the Hospital and for private cases. He felt keenly that the Hospital should be a school for the best possible education in nursing, and it was largely due to his constant co-operation that the Committee realised many of their ideals. He joined, too, in the work of a Society in Clifton with similar aims, which started and organised the first great Nursing Home with its staff of trained nurses, and is still carrying on a successful work in Chesterfield Place.

At the Bristol General Hospital he found one of his greatest interests in his duties as Dean for the medical students. His inspiring and methodical teaching drew to him a crowd of pupils, to whom he endeared himself by his constant care for their interests as well as by his scientific acumen and powers of exposition.

At the time he began professional life he saw that the opportûnities for an advance in Neurology were very great. Hughlings, Jackson, Ferrier, Gowers, and some Continental workers had opened up new methods of study. He threw himself with all his vigour into the localisation and pathological anatomy of nerve diseases, studying and utilising every case he met with, and spending his leisure hours in laboratory work. In this field his research and observations produced scientific gains of permanent value, some of which he found time to publish in the sixty neurological papers given with his other writings in the list appended ; but too many, alas ! remain buried in the carefully written note-books he accumulated. His studies on hysteria, on cord degeneration, and on the less known forms of paralyses are of great importance, but his devotion to Neurology did not prevent him from throwing new light on other medical subjects which came before him. Thus we owe to him a careful research on Trench Nephritis, which he saw among the soldiers at Southmead.

The Bristol Medical School, after more or less disorganisation during the eighteenth century, had been definitely revived some sixty years before Michell Clarke began to practice. It had been united to the new University College, but though vigorous it suffered under great disadvantages. The first of these was the impossibility of giving any degree or registrable qualification. There was also an almost entire absence of any endowments and of whole time teachers. One of the chief teachers complained that the dividend available for his course of lectures only amounted to eighteenpence. Still active teaching was carried on and a good average of successes in the London examinations was maintained. Michell Clarke lectured first in Physiology and then in Pathology, and as usual inspired his students with his own enthusiasm and scientific feeling.

An immense amount had to be done as funds came in to organise the work of the School more thoroughly. In the endless negotiations which followed and were continued when the Charter of the new University was obtained Michell Clarke's solid judgment and his skill in harmonising conflicting interests were of the utmost value. To a remarkable capacity for taking pains he joined a quiet but forcible way of stating his views, which were generally felt to be reasonable and always straightforward and disinterested.

When the University was an accomplished fact he became one of the Professors of Medicine, then Pro-Vice-Chancellor, member of the Council and of the Senate, and for a time Chairman of the Board of the Medical Faculty, all of which made further inroads on his time. His abilities had already been recognised by the Fellowship of the Royal College of Physicians (London) in 1896, and in 1917 he was placed on the Council of that College. Cambridge, too, had recognised his worth by making him an Examiner for the M.B. degree.

On the other hand, he had toiled for ten years for his brethren as Secretary of the Branch of the British Medical Association, with its arduous and often delicate duties. Then to help the Panel practitioners he served for other years on the Local Insurance Committee, when local feeling was running high; and unlike many men with a quarter of his work he gave a steady attendance at the scientific meetings of our Society and those of the British Medical Association, and contributed largely to the discussions.

His addresses as President of both Societies were characterised by their solid value and their happy phraseology.

The list given shows the large number of contributions he made to our *Journal,* and he was also an Editor of the *Quarterly Journal of Medicine,* of *Brain,* and the *Journal of Pathology.*

He gave active help, too, in assisting at the foundation of the Winsley Sanatorium, and to the Research Defence Society. As Consulting Physician to the Clifton Dispensary and a Governor of the Victoria Convalescent Home he found other fields of usefulness.

With all this he carried on a large consulting practice, which entailed long journeys over the West of England, as his scientific reputation and character were widely recognised.

When the war broke out he was at once called up as an *à la suite* officer and attached to the Southmead section of the Second Southern Hospital as Senior Physician, with the extra work of the Electrical Department. Summer and winter he daily covered the three-mile journey by 9 a.m., and before long as Lieut.-Colonel he was placed in charge of the administration of the entire section, which was raised to 1,020 beds. This would be a heavy task of itself for one man, since he had besides the soldiers a large number of officers undergoing treatment there, and a numerous staff, among whom he succeeded in maintaining harmonious relations. However, he found time to continue his researches and notes upon his cases, and as one of the Sisters said, " he was never too busy to hear anything we had to say." After many hours at Southmead he had to travel to Bedminster for his patients and lectures at the civil hospital there, and finally to find time and strength for his private patients and literary work.

For over three years this double strain went on. Meanwhile he was called to serve on the Local and on the Central War Committees, with the anxious and trying duty of selecting those doctors who could be best spared for the

Front. On the whole, the Committees succeeded in supplying the nation with a huge body of qualified men with the least possible disturbance of medical service for civilians; but it must have told heavily on a man so kind-hearted and sympathetic towards all his medical brethren.

Chance words at times showed how deeply the fluctuations of the war weighed on his patriotic feelings, but the grievous loss of his second son, who was killed at the Front, was borne with his usual quiet self-restraint.

We have not space to record his successes in golf, which he pursued with his usual thoroughness, rarely satisfying himself with his best performances, nor to describe his enjoyment of the social evenings with the century-old Medical Reading Society, where his huge appetite for new books was sometimes found to be a little embarrassing.

His brilliant scientific achievements, combined with an excellent judgment, and his quiet, modest demeanour, are known to all; but his fellow-workers realise sadly in looking back his remarkable energy and boundless capacity for work. Nothing strikes one more now than the great number of public duties which he carried out efficiently, unless it be the good temper and tact with which he preformed them. His whole life was one constant devotion to duty.

His scientific writings show his powers of observation and his indefatigable labour for the advancement of medicine, but it is to Michell Clarke, the man himself, to whom we wish to pay our tribute here. A man in all things straight, who never stooped to adopt a devious course to obtain his end. To his friends loyal, and to those against whom he might find himself, for the moment, opposed he was just. Looking back, we can remember no instance where he could be suspected of being unfairly biased by self-interest. A very active and busy man, he was never too busy to help anyone who came to him in a difficulty; he never spared himself in pains or time to right an injustice. His help was never showy, but it was admirably effective. It was a keen pleasure to him if he could himself slip away from the credit and thanks after matters were righted, but it has been astonishing to learn afterwards from the recipients what tactful and at the same time substantial help he gave to those in adversity.

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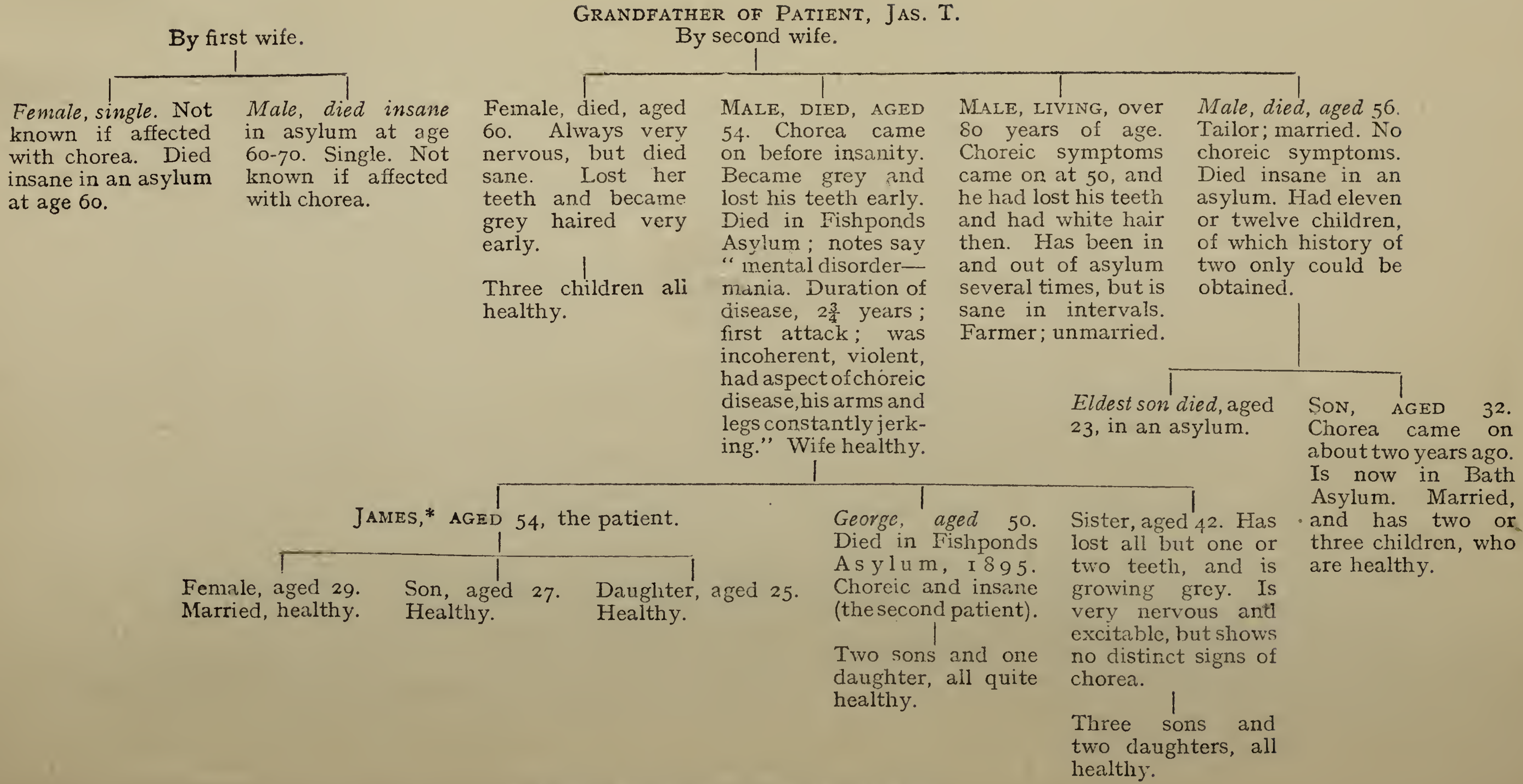
# I.—NEUROLOGICAL

# ON HUNTINGTON'S CHOREA.

THIS form of chorea, characterised by its appearing first in adult or late adult life, its tendency to affect several members of a family, to be inherited, and to end in insanity, is now well known, but cases are rarely met with in ordinary practice, and there have been few opportunities for *post-mortem* investigation of the morbid changes.

James T., a painter, aged 54, was admitted into the Bristol General Hospital for chorea and weakness, in September, 1895. The family history is given in the accompanying scheme. We could get no further back than the patient's grandfather, and no very definite account of him. The disease, however, appears to have come into the family through him, and not through either of his wives. On the male side there is also a history of rheumatism running through the family, and in both males and females a tendency to premature senility as shown by early greyness of the hair, and loss of the teeth is noticeable. Both the patients seen had the arcus senilis and well-marked degeneration of the arteries.

The patient was, like his brother, a small, thin man, looking older than his years, with marked arcus senilis and thickened, tortuous arteries. He had always worked hard, lived a regular and temperate life, had had no venereal disease, nor any bad illness. There was no history of any fright or great mental emotion, nor of any kind of fit or apoplectiform attack. There was no evidence of any past or present lead-poisoning. According to his wife the first symptom noticed was involuntarily stamping of the right foot five years previously ; two or three months later, twitchings came on in the right and then in the left arm ; soon all four limbs were affected. The patient himself said that he first noticed the twitchings on waking up one morning five years previously, and that they had persisted ever since, gradually growing worse. During the last six months he had been less intelligent, his memory had been failing, and his manner was changed. For two nights before he was admitted his wife had to sit up all night with him, as he was in a very excited state, looking wild, and talking constantly and incoherently. After admission he was quite quiet.



Grandfather of Patient, Jas. T.

By first wife.

- *Female, single.* Not known if affected with chorea. Died insane in an asylum at age 60.
- *Male, died insane* in asylum at age 60-70. Single. Not known if affected with chorea.

By second wife.

- Female, died, aged 60. Always very nervous, but died sane. Lost her teeth and became grey haired very early.
  - Three children all healthy.
- Male, died, aged 54. Chorea came on before insanity. Became grey and lost his teeth early. Died in Fishponds Asylum; notes say "mental disorder—mania. Duration of disease, 2¾ years; first attack; was incoherent, violent, had aspect of choreic disease, his arms and legs constantly jerking." Wife healthy.
  - James,* aged 54, the patient.
    - Female, aged 29. Married, healthy.
    - Son, aged 27. Healthy.
    - Daughter, aged 25. Healthy.
  - *George, aged* 50. Died in Fishponds Asylum, 1895. Choreic and insane (the second patient).
    - Two sons and one daughter, all quite healthy.
  - Sister, aged 42. Has lost all but one or two teeth, and is growing grey. Is very nervous and excitable, but shows no distinct signs of chorea.
    - Three sons and two daughters, all healthy.
- Male, living, over 80 years of age. Choreic symptoms came on at 50, and he had lost his teeth and had white hair then. Has been in and out of asylum several times, but is sane in intervals. Farmer; unmarried.
- *Male, died, aged* 56. Tailor; married. No choreic symptoms. Died insane in an asylum. Had eleven or twelve children, of which history of two only could be obtained.
  - *Eldest son died,* aged 23, in an asylum.
  - Son, aged 32. Chorea came on about two years ago. Is now in Bath Asylum. Married, and has two or three children, who are healthy.

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* A twin brother died when two days old.

*State on Admission.*—Abdominal and thoracic viscera normal. No cardiac murmurs ; heart sounds being normal. Urine normal. Constant choreic movements affect all the muscles of the trunk and limbs ; walking is difficult on account of them, but though the knees are often suddenly flexed, the spasms are not strong enough to throw him down. The facial muscles are affected, the patient making grimaces from time to time ; the tongue can be protruded, but is jerked backwards and forwards. The ocular muscles are unaffected. During voluntary movement the chorea becomes worse, and the hands and arms especially are agitated by spasmodic jerking movements when he tries to do anything with them. He can, however, feed himself if his food is cut up for him. Though voluntary actions are thus interfered with they are not distinctly ataxic. Muscular power rather weak ; dynamometer, 22 kilos., both for right and left hands. The muscles are small but show no wasting. Electrical reactions normal. The choreiform movements are constant during the waking hours, but cease entirely when he is asleep.

*Eyes.*—Pupils equal, of normal size, react well to light and accommodation. There was marked error of refraction ; on ophthalmoscopic examination the right optic disc was pale, with mottling of choroid on nasal side (Guttate choroiditis). Left optic disc was not so pale, choroidal changes were the same as in the right eye.

Superficial reflexes active, a well-marked "goose-skin reflex" is obtained over the skin of the chest and abdomen. Knee-jerks normal ; no ankle clonus ; front tap contraction present ; no muscular rigidity. Sensation to touch and pain normal, and power of localising sensations fairly good, but very slightly deficient over the hands. No affection of smell, taste or hearing. The functions of micturition and defæcation are natural. His face is somewhat expressionless, and he does not succeed in frowning or expressing surprise. He answers simple questions well, but if they are at all complicated he answers irrationally. He often repeats his statements. He has no delusions or hallucinations. His memory is defective and inaccurate. He sleeps well and has a good appetite. When in bed he can move his feet and legs well, and to any desired position, and there is no loss of the sense of position. The muscular sense appeared to be quite normal. He improved in nutrition during his stay in the hospital, but otherwise his condition was unchanged. He was given liq. arsenicalis in gradually increasing doses.

The younger brother of the above patient, George T., was in the Bristol Lunatic Asylum at the same time. I am greatly indebted to Dr. J. V. Blachford, Assistant Medical Officer to the Asylum, for notes of the case and of the *post-mortem* examination, and for the opportunity of seeing the patient and making the microscopical examination of the central nervous system. He was a small, thin, grey-haired man, who had for several years suffered from choreic movements affecting the limbs and trunk. He had never had syphilis. The diaphragm was unaffected, and he had no difficulty in swallowing. For three months previous to admission into the Asylum on July 1st, 1893, he was irritable and dangerous, and for twelve months his memory had been failing. He was demented, and had the delusion that the attendants were keeping back money that had been sent to him, but apart from this delusion he was quiet, and showed some amount of intelligence and power of memory. He answered questions as to his past life readily and correctly. The thoracic and abdominal viscera were normal; the heart being unaffected. The skin showed a condition of mild ichthyosis, best marked over the abdomen and thighs. The muscles though small showed no decided wasting. The knee-jerks were somewhat exaggerated, but there was no ankle clonus nor muscular rigidity. The pupils were equal and reacted well, the ocular movements were unaffected by spasm. He protruded his tongue spasmodically, and after much effort, and he walked with some difficulty on account of the muscular spasm. It is unnecessary to describe the choreiform movements, which were constant, and affected the muscles of the face, trunk and limbs, as they were precisely similar to those above described in the elder brother's case. They ceased entirely during sleep. In both cases the spasmodic movements were exactly like those of ordinary chorea. This patient died in the Asylum, after a few days' illness, of pneumonia, in November, 1895. The *post-mortem examination* was made twenty-seven hours after death by Dr. J. V. Blachford. There was lordosis of the lumbar spine. The *skull cap* showed a slight degree of transparency all over with some thinning at bregma. Pacchionian depressions well-marked. Diploë dense and scanty.

Measurements :

| | | |
|---|---|---|
| Average thickness .. | .. .. .. | 45 cm. |
| Diameters (Internal) | Antero-posterior | 17 cm. |
| | Transverse .. | 13 cm. |
| Circumferences .. | Antero-posterior | 31.2 cm. |
| | Transverse .. | 31.2 cm. |
| Horizontal .. | .. .. .. .. | 52 cm. |

Except for some injection of the pia-arachnoid the membranes were normal, and the pia-arachnoid stripped easily, and was not adherent to the cortex. The gyri appeared normal.

The grey matter over the motor area was well differentiated into a light intermediate band between two darker bands. The ventricles contained some excess of cerebro-spinal fluid. No abnormal changes were visible to the naked eye in the basal ganglia, pons, medulla, cerebellum, or spinal cord.

The whole brain weighed 44 ozs., the pons, medulla and cerebellum, 6 ozs. The xiphoid cartilage of the sternum was bifid. The *right lung* weighed 44½ ozs.; the lower lobe was in a state of red hepatization, portions sinking in water, the rest of the lung was intensely congested and œdematous. The *left lung* presented some fibrous contractions at the apex; there was some general congestion and œdema. The pleural cavities were obliterated by general adhesions. The other thoracic and abdominal viscera presented no morbid changes. The brain and spinal cord were hardened in Müller's fluid.

The following table gives the average of numerous measurements of the grey matter taken from the convexity of the convolutions in the several lobes of both cerebral hemispheres, after hardening about three months in Müller's fluid, together with those of a case reported by Dr. Charles L. Dana, and of the normal grey matter as given by him in his paper.[1]

The measurements are in millimetres.

| | This case. | | Dana's case. | Normal. |
|---|---|---|---|---|
| Frontal lobe | 2.50 | | 2.85 | 3.1 |
| Motor convolutions | 2.56 | Superior central | 2.2 | 2.75 |
| | | Parietal lobule | 2.2 | |
| | | Third central | 1.9 | |
| | | Lower central | 2.2 | 3.0 |
| Temporal lobe | 2.75 | | 3.2 and 3.1 | 3.1 |
| Occipital lobe | 2.58 | | 2.1 | 2.6 to 2.5 |

Sections of the fresh cerebral cortex were cut and stained by Bevan Lewis's method; others of the hardened brain from all parts of the cerebral cortex and from the cerebellum, after embedding in celloidin, were stained in hæmatoxylin and eosin, methylene blue, aniline blue-black, hæmatoxylin and picrofuchsin (Van Giesen), and by Weigert's method.

*Pia-mater.*—Vessels full, especially over the frontal and motor convolutions, their walls were, as a rule, normal, but, in a few instances, slightly thickened.

Convolutions of frontal lobe; vessels prominent, their walls healthy, and the perivascular spaces distended; in superficial layers of the cortex there were a few microscopic hæmorrhagic extravasations. The layer of small granule cells was narrow and stained badly. The small pyramidal cells showed morbid changes, many of them appearing shrunken, others deeply pigmented, their nuclei obscure and processes stunted. The large pyramidal cells and branched spindle or multipolar cells of the fifth layer appeared healthy.

In the motor convolutions the vessel-walls were healthy, but here and there a few red blood cells had escaped from the vessels. In a very few places the perivascular sheaths contained numerous leucocytes, which were passing into surrounding tissues. The small pyramidal cells showed the same changes as in the frontal region; a few of the large pyramidal cells contained much pigment obscuring the nucleus, but they were mostly normal. Cells of fifth layer normal. In both frontal and motor regions the number of small branched glia or interstitial cells seemed to be excessive.

In the occipital and temporo-sphenoidal lobes similar microscopic changes, but in less degree, were observed; in the former the glia cells were especially conspicuous, and in a few places wandering cells were present in the pericellular spaces around the nerve cells. Sections of the cerebellum, prepared by the above methods, showed injection of the small vessels of the cerebellar cortex, but otherwise presented no abnormal changes. The fibres in the white core of the convolutions, the cells of Purkinje, and of the granule layer appeared healthy. Unfortunately the nitrate of silver process was, for some reason, a failure in the cerebellum.

Sections were also prepared according to Dr. Berkeley's modification of Golgi's nitrate of silver method (*Brain*, vol. xviii., p. 473). This gave good results, with the drawback that in some cases the cell processes became broken across by the microtome knife in cutting the sections, and also that, like all the nitrate of silver processes, the staining was very capricious, only a proportion of the cells being stained, larger or smaller, as the case might be. Further, we do not know whether normal or abnormal cells best take the stain; so that so far as proportion of normal to abnormal cells is concerned, no conclusions can be drawn from the sections, but it was quite evident that there were a large number of morbid cells, and this stain also brought out the fact, observed in sections stained by the other methods, that the change is a partial one, healthy cells lying side by side with diseased ones. The most superficial layer of the cortex was healthy, the second layer stained very badly in all sections, and appeared narrow; those cells that were stained mostly appeared normal. The small pyramidal cells, as in the other sections, showed the most marked changes, many being shrunken, irregular in shape, their processes stunted with small nodose swellings upon them, and disappearance of the little "gemmulæ." No such swellings were seen, however, upon the axis cylinder processes, when these were visible. The large pyramidal cells, and the cells of the fifth layer, showed less marked changes, being, where stained, with some few exceptions, healthy. The nerve fibres of the white and grey matter and collaterals stained well and appeared healthy, both by the nitrate of silver and by Weigert's method. The glia cells were conspicuous in all parts of the cortex, especially in the frontal and motor regions, from their great number and large size, and appeared in many instances to be attached to pyramidal nerve cells, lying in immediate proximity to them. The occipital cortex was also rich in large, fine and richly-branched glia cells in its deep layer and subjacent stratum of white matter. In the parts of the cortex most affected by the morbid changes, the processes of the glia cells showed little nodose enlargements upon them, which I have not before observed. The pons and medulla appeared to be healthy. Spinal cord: grey matter in all parts normal; nerve cells in all parts healthy. The pia-mater was thickened, and there was a slight increase of the processes running into the cord from it, and of the neuroglia throughout the cord. No system-degenerations were present, the white matter being otherwise healthy.

It should have been mentioned above that the fibres in the white centre of the cerebral convolutions appeared healthy, the vessels in parts, but not universally, much injected. The glia cells were conspicuous and abundant throughout all sections. No further changes were noted in the white matter.

To sum up, the morbid change consisted in a widespread but partial degeneration of the cells of the cerebral cortex, especially the cells of the second and third layer, most marked in the frontal and motor convolutions, together with an increased amount of interstitial tissue and number of neuroglia cells.

In this family males have been chiefly affected. It will be noticed that the first patient showed evidence of mental affection; and that in the case of the sons of the patient's youngest uncle, both insanity and chorea have come on at an earlier age than in the others. According to Diller and Suckling, the disease comes at an earlier age in each generation, but this is by no means always the case. Wharton Sinkler (*Journal of Nervous and Mental Disease*, 1889) states that the disease may skip a generation.

Another case of this disease was under my care in the

Bristol Hospital in 1893. In this patient, a compositor, 46 years of age, the family history could not be fully obtained, but so far as could be ascertained, the tendency to insanity was less marked. His father was affected with choreiform movements, which came on two or three years before his death at 42 years of age; he was a temperate man, and was killed by falling from the roof of a house; the spasmodic affection of the muscles was said to have been the cause of the fall. The patient had two brothers and two sisters alive and well; two other sisters are affected with choreiform movements, one of the latter is in the workhouse, and is said to be crazy: her children are mentally defective, the Board-school teachers finding it impossible to teach them. There is no other case of insanity in the family. The patient himself used to drink at one time, but had been a teetotaller for twelve years. The illness began with loss of power in the legs, then the twitchings came on, and soon extended to all parts of the body. He also suffered from dyspepsia, and occasionally from attacks of frequent micturition. He was grey, poorly nourished, and looked ten years older than his age. The thoracic and abdominal organs were healthy. Heart of normal size, and the sounds normal. His face was rather expressionless; he spoke slowly and indistinctly, with a somewhat slurred utterance. Intelligence defective; memory very bad, and inaccurate; he showed a marked want of power of sustained attention, and answered questions badly, wandering off to other subjects.

The muscular system generally was only moderately well developed; there was no wasting, the muscles being well nourished, but flabby and weak. No rigidity, nor excessive muscular irritability to percussion. The dynamometer gave 21 kilos. right, and the same left hand. No fibrillary tremor. No paralysis. The muscles of head, neck, arms, and legs, and to less extent those of trunk, were agitated by constant spasms, in their general characters exactly resembling those of ordinary chorea, but rather more sudden and shock-like. These choreiform movements ceased during sleep, were aggravated by movement, or by talking; when lying down his head was occasionally suddenly raised up from the pillow. The movements interfere with walking, and have caused him to fall down. The facial muscles were affected, and those of the eyelids, but not of the eyeball. He protruded the tongue well, and had no difficulty in swallowing. The respiratory movements were occasionally noted to be a little irregular. There was no inco-ordination of movement.

The special senses were unaffected; sensation of all forms was normal, except that there was some loss of the temperature sense over the feet. Knee-jerks normal. Superficial reflexes; cremasteric and right abdominal not obtained, others present, plantar exaggerated. Pupils normal, equal in size, reacted well to light and accommodation. The temperature was constantly sub-normal, 97° to 97·5°. The bowels acted regularly.

This patient's daughter, aged 14, was said by him to be suffering from the same disease; but I saw her, and found that she was affected with diplegia and athetosis, most marked on the right side of the body, and the result of injury to the brain during birth. This bears out an observation in the *Lancet* (December 21st, 1895), "that this is almost invariably the actual condition in cases of so-called congenital chorea, so that the term is probably a misnomer, and the movements would be more correctly described as those of athetosis."

In a paper by Dr. E. S. Reynolds (*Med. Chron.*, vol. xvi., p. 21) will be found an excellent account of several cases, with references to the history and literature of the subject.

Important contributions to the study of the pathological anatomy of the disease have been made recently. Menzies

(*Jour. Mental Science*, October, 1892, and January, 1893) describes two families: in the first, 25 persons out of 100 traced were affected, the average age of onset was 27.6 years, and of death 43.7 years. In the second family: 13 persons out of 74 suffered, the average age of onset being 37.2 years, and of death 54 years. He concludes that the disease may descend from either parent to either sex, but that males are more commonly affected.

The *post-mortem* changes in the brain were slight coarseness of neuroglia, thickening of vessels, cell-degeneration, and, in hardened specimens, a few spider cells; in the cord, a diminution in the cells of Clarke's column, slight sclerosis of the ascending antero-lateral tract in all parts, and sclerosis of the posterior columns in the cervical region.

Oppenheim (*Centralb. f. innere Medicin*, 1894, p. 918) reports two cases: (1) a man who died of apoplexy, aged 75, in whom the disease had lasted sixteen years; and (2) a woman, who died of influenza, aged 56, in whom the duration was five years. There was a history of heredity, but I find no mention of insanity. *Post-mortem*, the heart was healthy in each case. In the brain the gyri were narrowed, and the sulci broadened in the motor, parietal and occipital regions; in these regions there were foci of hemorrhagic infiltration in recent, fibrillar in later, stages in the sub-cortical layer. In the cortex, the small round cells next below the uppermost layer were deficient in number. The pyramidal (? large) cells were normal. The basal ganglia were normal. In the cord there was increase in the neuroglia cells and fibres, chiefly in the lateral columns; these changes he does not regard as secondary to the cerebral lesions, as they are not systematic, and further, affect only the neuroglia and vessels. The peripheral nerves examined were found degenerated; and this he attributes in the first case to old age, in the second to influenza. He thinks the essential morbid condition to be a miliary disseminated encephalitis, cortical and sub-cortical, followed by atrophy of the cortex.

Dr. Charles L. Dana's (*Jour. of Nervous and Mental Disease*, vol. xx., p. 565) patient was a man in whom symptoms first appeared at the age of 33, and who died of typhoid fever at 37. The case constituted a transmission through females to the fifth generation. The convolutions of the brain showed anomalies in an interruption of the fissure of Rolando, and absence of the superior "*pli de passage.*" There was a general thinning of the grey matter, most marked over the central convolutions; areas of cell-degeneration, the angular and small pyramidal layers being most affected, the cell-defect being primary, the vascular changes secondary. He considers the disease belongs to teratology, being an innate defect in cell structure.

Kronthal and Kalischer (Virchow's *Archiv.*, Bd., cxxxix., Abs. in *Neurol. Centralb.*, May 15th, 1895), on the basis of the examination of three cases of chronic hereditary progressive chorea, conclude that the morbid process in Huntington's chorea consists in diffuse, rarely circumscribed, changes in the cortex of the brain; these are essentially disease of the vessel walls, increase of nuclei, cell accumulations, small hemorrhages, and increase of the interstitial framework; whilst the nervous elements are only slightly affected.

There seems then to be no doubt that the cerebral cortex, especially of the motor convolutions, is the seat of disease; the chief difference of opinion being as to whether the primary change is in the nerve cells themselves or in the supporting tissue. So far as my own sections go they point to a degeneration of the nerve cells, with a concomitant increase of the neuroglia.

Changes of a similar nature to those above described, but less marked, have been observed in cases of severe chorea of the ordinary type. Severe cases of ordinary chorea occasionally end in mania. In a girl, who suffered from an acute attack of extremely severe chorea, which became complicated with acute mania, and who died from exhaustion, I found, *post-mortem*, intense congestion of the small arteries and capillaries of the cerebral cortex. The bright injection of the vessels was obvious to the naked eye, and, under the microscope, sections of the cortex showed injected capillaries in extraordinary abundance, with some minute hæmorrhagic extravasations and cell-exudation, most marked over the motor area. The vessels of the basal ganglia and pons were also injected, but in much less degree.

The identical character of the spasms in cases of Huntington's chorea, and of ordinary chorea, points to affection of the same part or parts of the central nervous system in both cases. The severity, long duration and intractability of the symptoms in the former should render the recognition of the underlying lesion more easy, because the morbid changes would naturally be more extensive. The *post-mortem* changes above described indicate the cerebral cortex, especially of the motor convolutions, as the seat of the morbid change. The conclusion seems to be that all forms of chorea are due to disturbance in this region of the brain, although in each form the exciting cause of this disturbance is probably of a different nature, and the precise nature of the resulting alterations and capability of recovery vary accordingly.

In conclusion, I must express my best thanks to Mr. James Taylor for his kindness in making many excellent photographs of my sections, and to my clinical clerk, Mr. F. P. Mackie, for taking much trouble in investigating the history of the family above recorded.

## REFERENCE.

[1] *Journal of Nervous and Mental Disease*, vol. xx., p. 577.

# ON THE SPINAL CORD DEGENERATIONS IN ANÆMIA.

The exact relationship of anæmia to the degenerations in the spinal cord which are comprised under the various terms, "diffuse degeneration," "combined sclerosis," and "subacute combined sclerosis" of the cord, is still a matter about which there is considerable difference of opinion. From a clinical standpoint, anæmia may be associated with degeneration of the spinal cord in at least three ways: (1) it may distinctly precede the spinal changes for a longer or shorter time; (2) it may accompany them from the first, and proceed *pari passu* with them; or (3) it may appear late in the course of the cord affection, just as it often occurs in the later stages of any chronic illness. In the last instance, the anæmia is not as a rule so profound as in the other two. It should be added that in any case the anæmia may from time to time undergo considerable remissions, and occasionally be cured.

Although the subject is not a new one, many cases having been published, as it is still to a certain extent *sub judice*, the following cases, which belong entirely to the first group, where anæmia predominates over and precedes the spinal symptoms, and which illustrate both the early stages of the degeneration in the posterior columns of the cord and also their later development, have seemed to me not unworthy of record. I wish to emphasise that this paper deals only with cases in which the cord changes were, so far as one could judge, secondary to antecedent severe anæmia. In two of them disease of the cord was not suspected during life, and in all the anæmia was of considerable duration. It is not, therefore, a question in these cases of anæmia appearing in the course of primary chronic spinal cord disease. The second case is of especial interest, as I was enabled to watch it throughout the whole course of the illness; it presents the cord affection in an early stage, and is further interesting in that the anæmia was cured, and the cord changes had apparently ceased to advance.

With regard to the form of anæmia present in these and similar instances it is now established that it is by no means only, nor even most often, pernicious anæmia. In the published cases there is a lack of exact observations on the blood, and I regret that this fault unavoidably attaches to one of two of the following reports.

The first case was the first example in which the slighter change in the cord came under my observation, and appeared to represent the earliest stage in the cord affection of anæmia, but as the patient was only under observation during a short and fatal illness this was not certain. The correspondence of the lesion, though in a less advanced form, with that in Case 2, in which, as will be seen, there is no doubt that the degeneration is in the early stage, proves, however, that this first case shows the commencement of the cord lesion of anæmia.

Case 1.—The patient was a man, aged 26, who was admitted into the Bristol General Hospital, under Dr. Harrison, for pneumonia, and died a few days later. He was profoundly anæmic; examination of the blood gave red cells 660,000 to cmm., irregular in size and shape; hæmoglobin, 16 per cent.; blood decimal about $\frac{16}{13}$.

Besides the ordinary lesions of pneumonia and general anæmia of all the organs the chief changes found *post-mortem* were as follows. The non-consolidated areas of the lungs were rusty in colour; the heart small, but not fatty; the pancreas somewhat indurated; the mucous membrane of the small intestines thin, and in parts atrophic; Peyer's patches inconspicuous; the intestinal mucosa nowhere gave a pink colour with mercuric chloride solution ; no iron reaction in liver, spleen, or kidney.

The brain and spinal cord were apparently healthy, except that they were very anæmic.

Microscopic examination of the organs showed no noteworthy changes, except in the spinal cord. Sections were made of all parts of the cord, and exhibited partial degeneration of the posterior columns, entirely confined to the cervical portion, and not quite extending to the lower limit of that region.

The extent of the degeneration was most extensive at the level of the third and fourth cervical roots, occupying the greater portion of the central parts of the posterior columns, not affecting, however, the anterior and posterior extremities of the column of Goll, and leaving an unaffected zone of varying width on the dorsal surface of the cord, and lining the posterior commissure and posterior cornua. At the level of the fifth and sixth cervical the degeneration formed on each side a narrow truncated area, the broad end dorsally, in the lateral borde of the posterior median, and mesial part of the postero-external, columns. The posterior roots were normal, and there was no evidence of the entrance of degenerated fibres from them into the cord. Sections stained by Marchi's method showed a few scattered degenerated fibres in those parts of the posterior columns which, by the Pal-Weigert stain, appeared healthy, and also a very few in the lateral columns ; both sets in the cervical region only.

The grey matter and other parts of the cord were normal.

CASE 2.—*Profound anæmia, three and a half years' duration ; paræsthesiæ and paresis of legs after two years ; recovery from anæmia ; death from gangrene of lung following pneumonia ; post-mortem, stationary changes in cord.*

J.S., aged 28, gardener. First admitted to hospital March 29th, 1900. Family history good, both parents alive and well, and two brothers and three sisters are in good health.

He has never had any bad illness, nor suffered from anæmia previously. He has not had syphilis.

In 1898 he had a severe scalp wound which bled profusely, and about a year later he had profuse epistaxis from a blow from a stone.

For nine months he had been gradually losing strength, and had become anæmic. On exertion he had a sensation of tightness across the epigastrium, and pains in the back and legs. The feet and ankles became swollen towards night. For a week previous to admission he had been obliged to take to bed.

He was very pale in appearance ; there was no jaundice.

The pulse, 92, was soft and compressible, the tongue red and clean. Many of the teeth were carious.

The lungs were normal; systolic murmurs were audible at the base and apex of the heart, and over the great vessels. The lower edge of the liver could be felt, and the tip of the spleen came just below the costal margin.

The pulsations of the abdominal aorta were very plainly felt.

The urine was acid; sp. gr. 1021; it contained a trace of albumin, no sugar, and showed a faint band of urobilin.

He was given iron and arsenic, and kept at rest in bed, and on this treatment he steadily improved. In June he left the hospital much better, but with still a trace of albumin in the urine, and tendency to œdema of the feet.

He returned and was re-admitted on April 25th, 1901. He said that he had kept fairly well during the year, but had failed very much in the last six weeks. Since the beginning of the illness the slightest exertion had given him palpitation. Additional symptoms now were: twitching of the muscles of the legs at night, defective smell and taste, vomiting in the morning, a feeling of numbness in the fingers and toes and loss of flesh. On examination he was well nourished; he was anæmic, but had not the lemon tint of pernicious anæmia; the pulse was 84, very compressible. The organs were in the same condition as previously. The tip of the spleen could just be felt. The knee-jerks and other reflexes were normal. The colon again contained scybala. The twitching of the leg muscles sometimes prevented sleep. The amount of urine passed daily was from twenty to forty ounces, it still contained a trace of albumin, and showed a moderately well-marked but diffuse urobilin band. Specific gravity 1025. There were no hemorrhages in the fundus oculi, which was anæmic, but otherwise normal in both eyes.

From June 7th to 17th he was not so well, the temperature was raised to 100° with slight diurnal variations, and he was very weak, not being able to wash himself or get out of bed. There was also an increase of the urobilin in the urine, and the spleen became slightly larger.

From June 17th the condition of the blood gradually improved, he looked better, the spleen diminished in size, and the urobilin band practically disappeared from the urine. The skin was somewhat dark and pigmented. The muscles of the legs were weak and flabby, but not tender or distinctly wasted. Sensation was unaffected; the plantar reflexes were flexor in type, and feeble.

He now left the hospital, and was next admitted on April 3rd, 1902. He had kept in fair health until the beginning of the year, when he began to get very weak and to suffer from shortness of breath, palpitation, and giddiness.

He had a red flush on the cheeks, but the mucous membranes and the rest of the skin were pale. Over the chest, back, and limbs small round pigmented spots and petechiæ were fairly numerous. The pulse was regular, 76, full, and somewhat tense. The tongue was red and clean.

Physical examination showed that the condition of the organs was the same as on previous occasions, except that the liver was not felt. The spleen was slightly enlarged. The urine sometimes contained a faint trace of albumin. By Jaffé's test it appeared to contain a large quantity of indican, and with the spectroscope it showed a diffuse, but not intense or sharply-defined urobilin band. There were also crystals of oxalates and phosphates.

During April and May his condition remained much the same ; he was very weak and had no appetite. The temperature rose occasionally to 100° F. at night, falling a degree or so in the morning. He complained of numbness and tingling in the feet, especially in the right foot. Both optic discs and fundi were very pale, but there were no signs of past or present hemorrhages. Towards the end of May he had a very bad attack of diarrhœa, after this he improved and left the hospital at the end of June without any fresh symptoms. It should be added that at the beginning of June he was not so well, suffering much from pains in the back, abdomen, and limbs, and there was a rise of temperature to over 100° F. on several successive nights. The tingling and numbness in the legs and feet continued, but without objective loss of sensation, except that he had some difficulty in feeling a hot test-tube as hot. He was seen as an out-patient in October, and was then keeping well, though not very strong. His cheeks were red and his face generally a good colour ; his chief complaint was of tingling and numbness in the feet and legs, and of some weakness. He attended as an out-patient for about two months. He could walk a fair distance, and there was nothing remarkable about his gait. The knee-jerks were present, not very active ; there was no wasting of muscles and no rigidity. Plantar reflexes weak and flexor in type. Very slight defect of sensibility to touch and prick over the lower extremities, especially on the feet.

The condition of the blood at this date showed very marked improvement.

He was not seen again until May 14th, 1903, when he was brought up to the hospital in an almost collapsed condition. He was very drowsy, and at first refused to take any nourishment.

There were signs of consolidation of the lower lobe of the left lung, and the breath and sputum were horribly offensive. The pulse was 120, very feeble, and the heart's sounds almost inaudible.

The temperature was irregular, soon after admission it rose to 103°, and for some days afterwards varied between 100° and 104°. He was very dusky in colour. The abdomen was retracted, the spleen was not felt. The urine was retained, a specimen withdrawn by catheter was acid, sp. gr. 1,030, with much albumin and many hyaline casts.

The lung symptoms steadily developed, and he died from heart failure ten days after admission.

During this last stay in hospital he was too ill to make a satisfactory examination of the nervous system possible; he came in with a sacral bed-sore (he was very ill at home for three weeks before admission), and one developed on the right heel shortly afterwards. So far as could be made out there was no decided loss of sensation to touch or prick over the lower extremities, no spastic contracture of them, and he could move them well. There was general wasting.

The following table gives the condition of the blood at intervals during the whole course of the illness:—

*Chart of Blood.*

| | Red blood corpuscles. | Hæmoglobin. | Blood decimal. | White cells. | |
|---|---|---|---|---|---|
| March 27, 1900 | 2,800,000 | 50 per cent. | 1 | 10,000 | Slight increase in eosinophiles in lymphocytes and mononuclear cells. |
| June 11, 1900 | 3,000,000 | 55 per cent. | $\frac{11}{12}$ | 7,000 | |
| May, 1901 | 2,240,000 | 32 per cent. | $\frac{16}{25}$ | 8,000 | Lymphocytes and mononuclears increased somewhat. Eosinophiles in normal proportion. |
| June 3, 1901 | 2,000,000 | 38 per cent. | $\frac{19}{20}$ | | |
| June 20, 1901 | 1,700,000 | 34 per cent. | 1 | | |
| July 15, 1901 | 3,800,000 | 52 per cent. | $\frac{15}{19}$ | 5,000 | |
| May 23, 1902 | 2,000,000 | 30 per cent. | $\frac{3}{4}$ | 4,000 | Differential count showed normal proportion between kinds of white cells. |
| Oct. 16, 1902 | 3,420,000 | 48 per cent. | $\frac{12}{17}$ | 4,000 | |
| May 15, 1903 | 4,100,000 | 80 per cent. | 1 | 20,000 | Specific gravity 1,061. A polymorphonuclear leucocytosis due to pneumonic changes. |
| May 20, 1903 | 4,100,000 | 75 per cent. | — | 20,000 | |

With regard to the red cells, at the beginning of the illness, and at each subsequent relapse, there were numerous microcytes, macrocytes, and poikilocytes, with a small number of normoblasts. As the condition improved on each occasion, the red cells tended to return to the normal shape and size. No megaloblasts were seen at any stage. The *post-mortem* appearances were briefly: gangrene of lower lobe of left lung; general bronchitis; congestion of base of right lung; heart muscle pale and flabby, but not fatty; congestion of liver and spleen; kidneys intensely congested and indurated; marrow in ribs, sternum, and shaft of one tibia red in colour.

Sections of the various organs were stained with hæmatoxylin and eosin, hæmatoxylin and rubin and eosin, and osmic acid and carmine.

The following is a short summary of the microscopical changes:—

*Heart.*—No fatty change; increase of pigment round nuclei of muscle fibres.

*Liver.*—Congestion; cloudy swelling of liver cells, many of which showed vacuolation.

*Spleen.*—Intense injection; some excess of large pale cells in sinuses, apparently due to proliferation of cells lining them.

*Kidney.*—Chronic glomerular nephritis of moderate extent, affecting the convoluted tubes but slightly.

*Marrow.*—Excess of polymorphonuclear cells.

No iron reaction given by any organ.

The brain was normal.

*Spinal cord.*—By the Pal-Weigert stain the posterior columns showed a degeneration which, beginning in the upper dorsal region as a small area of degeneration in the posterior and central parts of Goll's column, extended throughout the cervical portion of the cord. In the cervical region the degeneration was almost entirely one of Goll's column, except that it extended a little on the dorsal surface of the cord to involve the posterior end of the postero-external columns. The degenerated areas gave no reaction with Marchi's stain, most probably because the degeneration was of old standing, but in them were minute areas or cavities, from which the nerve fibres had disappeared. This same appearance was also noticed to a very small degree in the crossed pyramidal tracts for the extent of two or three segments in the upper dorsal region of cord only. The other parts of the cord were normal, as were also the grey matter, the anterior horn cells, and both anterior and posterior roots at all levels.

The interest of this case lies in the circumstance that the patient had recovered from his long-continued anæmia, and died from an accidental lung affection. Further, the changes in the cord had not advanced very far, and apparently had ceased to extend; I think this is also the reason of the slight affection of the postero-external columns. The microscopic appearances and the clinical symptoms both point to the stationary character of the cord lesion. If this inference is correct, then the case illustrates the close connection of the cord changes with anæmia, and their dependence upon the latter. As showing the completenesss of the recovery from anæmia, the fact that the hæmato-poietic organs were able to cope with the strain of the fatal illness is important. Although in some respects, especially in the recurring episodes of blood destruction, the illness resembled pernicious anæmia, yet in most of its features, and notably in the fact of such complete recovery, it did not correspond with the latter condition. The state of the blood fairly corresponds to Cabot's third grade of secondary anæmia, the leucocytosis, which accompanies this form in the severer cases, not being very pronounced.

Case 3.—John C., aged 45, admitted under Dr. Harrison. The clinical notes of this case were very brief; it appears to have been entered in the hospital records as pernicious anæmia, but the notes, blood changes, and *post-mortem* appearances hardly bear out this diagnosis. The illness began nine months previously to admission with an attack of pneumonia, followed by severe anæmia, and for the last four months of this time he had had various paræsthesiæ, numbness and tingling in the hands and feet, with weakness of the limbs. There was no absolute paralysis, nor anæsthesia. He died of bronchitis, for which he came into the hospital, nine days after admission.

The blood examination gave 2,600,000 red cells; hæmoglobin 30 per cent.; blood decimal $\frac{3}{5}$. No increase of white cells. Red corpuscles varied in size; many poikilocytes; no megaloblasts or normoblasts.

*Post-mortem.*—The fat was bright yellow; some yellow transudate in serous cavities gave no urobilin band; general bronchitis; œdema of bases of lungs; no fatty changes present in the heart or other organs; kidneys very pale but not fatty; the liver and kidney gave a faint iron reaction, but not the spleen; the latter weighed 4 ozs., and appeared healthy; marrow healthy; small intestine showed patches of catarrh, no pink colour was obtained by treatment of mucous membrane with mercuric chloride solution; brain and cord healthy in appearance, except for the general anæmia, which affected every organ.

The above findings were confirmed by microscopical examination. The cord showed a more advanced degeneration of the posterior columns than in the two preceding cases, though here also the columns of Goll were most affected. The degeneration extended regularly, though slightly patchy in character, from the medulla to the level of the first lumbar roots, but not below this, being most intense in the cervical and upper dorsal regions. In the former the most intense degeneration occurred along the boundary between the postero-median and postero-external columns; it affected the greater part of these columns, leaving a marginal zone of varying extent, lining the posterior commissure and cornua and the dorsal surface of cord, free from disease. In the dorsal region the degeneration was rather less extensive, the marginal area being broader; the diseased part gradually diminished in passing down the cord until it became a very small patch on each side at the first lumbar segment, below which it could not be traced.

In sections stained by Marchi's method a few scattered degenerated fibres were seen, as in Case 1, in the lateral columns (position of pyramidal tracts), and in the postero-external columns, in areas which by the Pal-Weigert stain appeared normal.

The degenerated fibres, as in the other cases, could be traced upwards to the posterior nuclei, chiefly nucleus gracilis, in the medulla, in which they ended. The grey matter, posterior roots and other parts of the cord were healthy. For vessels, see general description.

Case 4.—This patient was one who died of anæmia in the hospital; but unfortunately I have no notes of the case, nor of the condition of the blood.

A complete examination was made of the spinal cord, brain, and some of the peripheral nerves. The brain and the nerves were healthy. In the cord degeneration of the posterior columns was found, extending through the cervical and dorsal regions, and through the lumbar as low as the level of the fourth lumbar roots, where it ended, not involving the sacral region. The degeneration in this case is more extensive than in the foregoing cases, and corresponds in this respect more to Case 5. It was, however, as in the milder cases, most extensive in the cervical region and upper dorsal region, in which the whole of the posterior columns were affected, except a very narrow bounding rim of healthy tissue. In the lower dorsal and lumbar regions this margin was larger.

In the lateral columns in the upper and mid-dorsal regions of the cord there was a small area of degeneration on each side in the position of the pyramidal tracts, but this did not extend into the other parts of the cord.

Case 5 is published in full in the *British Medical Journal*, 1897, vol. ii., p. 326, with figures of the spinal cord degenerations. In this case the condition was apparently one of pernicious anæmia. She died nine days after admission to the hospital. The duration of illness was twelve months, during the *last four months* of which she had suffered from increasing weakness of the legs, with a feeling of deadness in them; when admitted there was some loss of motor power, no affection of sensation, and the plantar and deep reflexes were active.

The blood examination on admission gave red corpuscles 870,000, many poikilocytes, macrocytes, microcytes, and some normoblasts. White corpuscles 10,000, the increase being due almost entirely to polymorphonuclear cells. Hæmoglobin 30 per cent.; blood decimal ·6. Seven days later red cells 830,000; whites 30,000; hæmoglobin 25 per cent. The changes in the cord were most advanced in this case, as a reference to the figures will show; briefly they consisted in a fairly complete degeneration, though somewhat patchy in distribution, of the posterior columns extending the whole length of the cord, ending above in the nuclei of the posterior columns in the medulla, and in the lower dorsal and upper lumbar region by a small area of degeneration in the posterior part of the left lateral column.

This series of cases, I think, shows that the spinal degeneration which occurs as a secondary change in profound anæmia, and has been found and described by many observers, begins in the posterior columns and first in the cervical and upper dorsal regions of the cord. Further, that in cases which die from some cause in an early stage of the cord disease, the affection may be unsuspected during life, and will be found limited to this region after death. In more advanced cases the posterior columns are involved almost throughout the cord, and the disease is then most extensive in the region in which it first begins, affecting here the whole of the posterior colums except a narrow rim of tissue on the dorsal surface and lining the posterior commissure and posterior horns: in the lumbar and sacral regions rarely spreading to so great an extent. These changes, though fairly regular, and possibly indicating that the fibres of the posterior columns which run the longest course are earliest degenerated, do not exactly map out special tracts, but are somewhat patchy in distribution, often varying at different levels for no obvious reason. The posterior roots do not seem to be affected. The appearances in some instances suggest some relation to the vessels, as the degeneration often seems to begin in the terminal distribution of the small artery that runs into the cord along the septum between the column of Goll and the postero-external column, that is to say, a small area about midway between the anterior and posterior ends of Goll's columns, involving slightly the postero-external columns. This relation is, however, though suggestive, not constant, and therefore no undue stress can be laid upon it.

In the cases in which the posterior column changes are most marked a patch of degeneration is also to be seen, either on one side or both, in the lateral columns in the position of the crossed pyramidal tract; this, again, is most evident in the cervico-dorsal or upper dorsal regions, but in one case appeared in the dorsi-lumbar region. It is more patchy and less regular even than the degeneration in the posterior columns, and does not extend over so great a length of the cord, in mild cases being limited to a few segments.[1]

It must be added to this that though the Pal-Weigert stain may indicate degeneration limited to the above situations, sections stained by the Marchi method often show a few scattered degenerated fibres occurring singly in a much wider distribution in the posterior, lateral, and occasionally a very few in the anterior, columns. Fibres stained black by this method also appear, if the case is a recent one, in the areas which by the Pal-Weigert stain appear to be already degenerated. As regards the finer changes they may be said to be practically identical with those described by Dr. Risien Russell in cases of "subacute combined degeneration" of the cord. The vacuolation resulting from the destruction and dropping out of nerve fibres is generally well seen.

In the degenerated areas there is an increase of the neuroglial framework, the vessels often show greatly thickened walls, and sometimes hyaline degeneration of them. In some of my sections the overgrowth of neuroglia seems to have been more extensive than was met with by Drs. Putnam and Taylor.[2] The older the patch the greater seems to be the sclerosis, the denser the structure of the part, and the less marked the vacuolated spaces, as if the tissues had contracted. In such cases the increased connective tissue may appear to spread directly from the vessel walls, and sometimes the leucocytal infiltration is seen around the latter. These changes seem to me to be entirely secondary to the parenchymatous degeneration of nerve fibres, and although, as alluded to above, this degeneration shows an apparent relation to vascular distribution, I should not attach further weight to this than that it may possibly indicate the route of conveyance of a toxin.

In favour of the secondary nature of the vascular changes is the fact that they are not evident in regions where the nerve degeneration is slight (and recent), and, further, are not present in areas of the cord where the only evidence of disease lies in the presence of a few scattered degenerated fibres. I found no patches of myelitis in my cases. The grey matter and its contained cells showed no important changes, the only noticeable one being the not infrequent presence in the cells of the anterior horn and of Clarke's column of an unusual amount of pigment. This pigmentation is also mentioned by Putnam and Taylor. The meninges were in all cases unaffected, and the peripheral nerves, where examined, normal.

To turn to the clinical features of these cases, clinical symptoms may certainly be absent, and the lesions in the cord not even visible at the *post-mortem*, but only found after hardening and staining it. It is probable, therefore, that such degenerations in the cord are of more frequent occurrence in patients dying from anæmia than is generally supposed. As these changes are secondary and subsidiary to the general symptoms of severe anæmia, they may easily be overlooked, but my more recent experience is that a careful investigation will generally elicit some signs of the affection of the cord.

The most prominent clinical symptoms are certainly paræsthesiæ of various kinds, such as numbness, tingling, feelings of pricking, or of pins and needles, first appearing in the feet and legs. Later the hands and forearms may be affected, when a common complaint is that numbness or deadness of the fingers renders fine movements difficult. These paræsthesiæ vary much in intensity during the course of the illness. Objective disturbance of sensation is not marked, but in the late stages may consist of some deficient appreciation of all forms of sensation over the lower extremities. After these sensory symptoms weakness in the legs may follow, often in the sense that they feel heavy, and later still both arms and legs may be weak. A frequent and often troublesome symptom is twitching of the muscles, especially of the legs, and at night. The deep reflexes are present, ankle clonus is not obtained, and the plantar reflex, flexor in type, is sometimes difficult to get. The knee-jerk was absent towards the end of life in Case 2, but he could only be examined as he lay in bed.

There is no ataxy, and no incontinence of urine.

In relation to the clinical symptoms, I should like to briefly mention another case, though the diagnosis was not confirmed by a pathological examination.

The patient was a middle-aged man who suffered from a form of rhinitis, with a spongy condition of the nasal mucous membrane, which gave rise to recurrent attacks of profuse epistaxis. Under treatment in hospital he was invariably relieved, but after an interval, generally of considerable duration, six months to two years, he relapsed, and the attacks of epistaxis returned. This epistaxis led to moderately severe anæmia of the chlorotic type, as regards the ratio of red blood cells to hæmoglobin. He was thus under observation for anæmia at intervals for over five years. The following is the chart of the blood, which indicates a progressive deterioration of it :—

| | | | | |
|---|---|---|---|---|
| 1896. Jan. | 3,100,000 | 31 per cent. | | |
| (On leaving Hospital) March | 4,300,000 | 62 per cent. | | |
| 1899. Feb. | 2,400,000 | 25 per cent. | 10,250 | Many poikilocytes, normoblasts, small and large red corpuscles. |
| | | | Polymorphonuclears 69 per cent.<br>Small lymphocytes 23 per cent.<br>Large lymphocytes 4 per cent.<br>Eosinophiles 4 per cent. | Poikilocytes, normoblasts, micro- and macrocytes numerous. |
| 1900. July | 2,750,000 | 35 per cent. | 9,000<br>Differential count normal. | As before. |
| 1901. Feb. | 2,400,000 | 25 per cent. | 1,200 | |
| | | | Polymorphonuclears 67 per cent.<br>Small lymphocytes 23 per cent.<br>Large lymphocytes 8 per cent.<br>Eosinophiles 2 per cent. | As before. |

On the last occasion the anæmia only slightly improved under treatment, but on previous ones recovery was satisfactory, as in 1896, but I have not thought it necessary to give the actual blood counts each time.

Whilst in the hospital in July, 1900, he complained for the first time of various paræsthesiæ, especially tingling and numbness in the feet and legs ; and on his subsequent admission in 1901 these symptoms had very much increased, and were the source of great discomfort. He now complained of deadness or numbness of the hands and fingers, varying from time to time, and sometimes interfering with the performance of fine movements. There was no decided objective loss of sensation, although it was perhaps somewhat dull over the feet. He also complained of some weakness in the legs, so that he could not walk so far as formerly. There was no ataxy and no muscular wasting; the knee-jerks were slightly exaggerated.

I have not been able to trace this man, but I have no doubt that the case was one of the same kind, *i.e.* of a spinal lesion developing secondarily to repeated attacks of severe anæmia.

Hemorrhage as the cause of anæmia in such cases deserves special mention, and is probably of importance; it occurred in two of my cases as the prominent etiological factor, and has been noticed in several others.[3]

The cases that I have described above form a fairly distinct group, and the changes in the cord occur in such a way as to show that they result from anæmia, and from forms of anæmia due to blood destruction. Though pernicious anæmia is one form which causes these cord lesions, it is by no means the only one. I am here taking pernicious anæmia in the ordinary sense of the term, though there is so much difference of opinion as to what actually constitutes pernicious anæmia that it is difficult to avoid confusion. In favour of the point that it is only when anæmia is due to blood destruction that these cord changes follow is the striking fact that they are not seen in chlorosis, of however long standing. A possible view of the pathology of these cases seems to me to be that of parenchymatous degeneration due to some toxin, possibly set free in the course of a pathological blood destruction, and therefore hæmolytic in origin. More extended observations on the blood, and on the precise character of the anæmia, would tend to elucidate the nature of the process.

In this particular group the cord changes often follow on so long a period of anæmia that it is difficult to suppose that the lesion is other than a secondary one, although it is possible that the cord changes might be due to the continued action of the same cause that has already produced anæmia, just as in those cases of cord degeneration and anæmia described by Dr. R. Russell and Dr. J. Taylor they suppose that both conditions are due to the same toxin.

It may be mentioned, in passing, that in pernicious anæmia lesions in the spinal cord of quite another kind sometimes occur, namely numerous small hemorrhages, chiefly in the grey matter. Such cases are rare[4]; the hemorrhages are to be compared with those found in the retina in this disease, and seem to me to have nothing to do with the cases now under consideration. There was no evidence in my sections that the degeneration started from any lesions of this kind.

The question now arises: Is there sufficient reason to put cases such as are considered in this paper, in which the cord changes distinctly follow or are secondary to profound anæmia of some duration, into a separate group, and to distinguish them from those in which similar lesions of the spinal cord occur, apart from anæmia; and further, what is their relation to the cases described by Risien Russell, Batten, and Collier[5] under the title of "Subacute Combined Sclerosis," and by Putnam and Taylor[6] and others, under the head of "Diffuse Degeneration of the Spinal Cord"? The latter writers say that "it seems to us too soon to make either clinical or pathological divisions in the general group of diffuse degenerations, and particularly to attempt the demonstrations of lesions peculiar to anæmia."

Such a division has been already attempted by Bastianelli in 1895, but his distinction, valuable as it is, is partly based on the acute or chronic course of the disease,[7] and will hardly hold good, for, as three of my cases show, and as other writers have also pointed out, the anæmic cases which, according to his classification, fall into the acute class, are, on the contrary, often chronic in course. I believe, however, he is correct in the view that, as a general rule, in the cases secondary to anæmia the cord changes are slighter, and most often limited to the posterior columns.

Without laying undue stress on the anatomical characters of these cases, it seems to me that there are good grounds, both clinical and pathological, for separating them from similar forms of degeneration of the cord, and that these are: (1) The presence of decided or severe anæmia as the first, or sometimes the only, sign of illness; preceding any evidence of spinal cord lesion. (2) Clinically symptoms and signs of disease of the cord are never very pronounced, and may be absent, though, possibly, in most cases they are present when looked for. (3) Anatomically the lesion is generally confined to the posterior columns, and, if it affects the lateral columns, only does so to a small extent. And (4) it differs in extent and distribution from *subacute combined sclerosis* or *diffuse degeneration of the cord* in the following ways, according as the disease in the latter case is slight or severe. (*a*) In the milder cases of diffuse degeneration the degenerations are more precisely limited to the neuronic systems of the cords; thus, in two cases under my own observation the columns of Goll were diseased from the lumbar region upwards to the medulla, and the crossed pyramidal and dorsal cerebellar tracts were similarly affected; whilst in (*b*) the more severe cases the degeneration is both much more extensive than in the cases considered in this paper, and also affects the periphery of the cord most, and appears to spread thence inwards, at any rate in the lateral and anterior columns.

On the other hand, it must be admitted that the microscopical details of the degeneration process appear to be similar in both groups, and further that there are cases which occupy an intermediate position, in which the cord changes are associated with profound anæmia, and are also very extensive in distribution. It seems to me that the chief difficulty lies in the nature of these intermediate cases.

In conclusion, although the evidence is not sufficient for a final classification, I think that a step in advance might be made by separating into two distinct groups (1) the cases of pronounced anæmia with lesions in the spinal cord of the character described in this paper, and with slight or absent clinical signs of this disease; and (2) those of subacute combined degeneration or diffuse degeneration of the cord in which there is no anæmia, or, if it is present, it is late and consecutive to the appearance of symptoms of cord disease, and in which also the pathological changes in the cord are more extensive and their symptoms pronounced, following more or less closely the course outlined by Drs. Russell, Batten, and Collier.

In support of this division it may be mentioned that in fifty cases of the latter kind collected by Drs. Putnam and Taylor, in only seven was there decided anæmia. Those cases which seem to combine the features of the two groups, in presenting both profound anæmia and widespread cord degeneration, I should propose to leave provisionally in a class by themselves pending further investigation.

## REFERENCES.

[1] A typical example of the affection of the pyramidal tract in these cases is figured in my paper in *Brit. Med. Journ.*, 1897, vol. ii., p. 326, fig. 3.

[2] "Diffuse Degeneration of the Spinal Cord," *J. Nerv. and Mental Dis.*, 1901.

[3] *Vide* Dr. James Taylor, "A Case of Subacute Combined Sclerosis," *Brain*, 1904, p. 34.

[4] For a case of this sort see *British Medical Journal*, 1897, vol. ii., p. 326.

[5] *Brain*, Spring, 1890.

[6] *J. Nerv. and Mental Dis.*, 1901.

[7] See J. Taylor, "A Case of Subacute Combined Sclerosis," *Brain*, Spring, 1904.

# ON SOME SYMPTOMS OF CEREBELLAR TUMOURS.

THE symptoms of cerebellar tumours to which I wish first to allude are those connected with disturbances of hearing. Affection of hearing not unfrequently occurs in cerebellar tumours, because they exert pressure upon the auditory tracts or nerves. It generally takes the form of impairment of hearing only, and is either unilateral or is more marked on the side of lesion. Associated with deafness may be tinnitus aurium, especially, according to Ferrier,[1] in connection with tumours of the middle lobe. It is not common, however, to get absolute and complete deafness as in the two following cases, in which it was also accompanied by very distressing tinnitus aurium. In these cases, moreover, the deafness and tinnitus long preceded the pathognomonic symptoms of cerebellar tumour, and it was on account of deafness that the patient first sought advice. By the time, however, that they came under my own observation there was in the first case commencing optic neuritis in one eye, and in the second inco-ordination of movement, symptoms incompatible with disease limited to the organs of hearing, but until these signs appeared the diagnosis must have been impossible.

CASE I.—The first patient, a man æt. 40, a clerk, I saw, through the kindness of Dr. Barclay J. Baron, in May, 1897. He was well nourished and healthy looking, but grey, and looked older than his years. He had never had syphilis nor any previous illness, except rheumatic fever at the age of 14. He complained chiefly and bitterly of noises in the ears—a constant roaring, a bell ringing, or gongs striking; these first came about six years ago, and have been constant ever since.

They were worse in a noise of any description, even talking increased them. They did not prevent sleep. He was stone deaf. Deafness came on in the right ear six years previously, and at that time the Eustachian tube was blocked. Dr. Baron tells me that he then treated him for double labyrinthine deafness with injections of pilocarpine. The left ear had gradually become deaf during the last six months. The noises in the ears preceded the deafness. He also complained of a feeling of uncertainty or unsteadiness of his legs. On this account he was nervous about going up or downstairs; the right leg was weaker and more uncertain. He had never fallen, and had not suffered from giddiness.

On examination he appeared to walk naturally and briskly; there was slight swaying on standing with the eyes shut, but he could walk forwards and backwards with his eyes closed. There was no paralysis of any cranial nerve. Swallowing normal. Speech rather rapid and monotonous, but natural. Pupils, right contracted and fixed; left dilated. They acted well to light, to accommodation, and consensually. There was fine horizontal nystagmus of both eyes in movements to either canthus, but not when at rest. There was some myopia. Right optic disc normal, left showed commencing neuritis. The visual fields, taste, and smell, were normal. No affection of sensation in any part of the body; no paralysis of the limbs or back; no muscular wasting; musculature poorly developed; electrical reactions normal. No rigidity. Knee-jerks present, but very defective, especially on the left side. Superficial reflexes normal. There was a fine constant tremor, not increased by movement, of arms and hands. Twitchings of the muscles of the legs occurred frequently, especially in the quadriceps extensor femoris. Micturition and defæcation normal. No tenderness over head or spine, and the latter showed no deformity. Mental powers normal; memory good. He is able to go on with his work.

November, 1897. When seen again condition unchanged, except that tinnitus was worse. He could walk twelve to fourteen miles, never fell, but occasionally felt uncertain on his legs; he was not giddy.

October, 1898. Condition rather worse; sight failing, especially in left eye; he feels generally weaker, and is more easily tired; he cannot walk so well as formerly, and has difficulty in walking in the dark and in keeping steady; he walks like one intoxicated. He is now slightly giddy, and has frontal and occipital headache. No vomiting. No ataxy of movement. There is a little difficulty in starting micturition. Right pupil small and fixed, left normal and active. Nystagmus same; no oculomotor or other cranial nerve paralysis. Visual fields normal. Marked double optic neuritis; most advanced on the left side. He had now an uncertain titubating (cerebellar) gait in walking backwards or with the eyes shut, but hardly noticeable in ordinary walking. No ataxy of arms or hands. Fine tremor of legs. Both knee-jerks absent.

In November, 1898, it was noted that his gait was decidedly ataxic, and he had a tendency to walk or fall to the right. He was slow and awkward in rising from a chair. The right leg seemed weaker than the left. The right grasp by dynamometer, 30; left, 37 kilos.

At the beginning of 1899 he saw Dr. Ferrier, who agreed with the diagnosis of cerebellar tumour. He stayed two months in the Queen Square Hospital, where Sir V. Horsley did a craniotomy, removing a large piece of bone low down on the right side below the level of the tentorium and of the occipital ridge.

This resulted in improvement of general symptoms, but in March, 1899, it was noted that he had a marked cerebellar gait, much worse when his eyes were closed, and he was not able to walk without a stick. Optic neuritis about the same in the left, better in the right eye. He suffered from attacks of temporary blindness, followed by intense headache and giddiness. Nystagmus was now most marked on looking to left. Other symptoms remained as before. A considerable soft, fluctuating, painless swelling about the size of half an orange had developed over the site of the trephine opening. After this date I saw him occasionally from time to time. The general course of his illness may be given very briefly. He remained stone deaf; the noises in his ears also troubled him, but were less than at first. The headache also improved. The optic neuritis cleared up, leaving a slightly atrophic condition of left disc but fairly good sight, so that he could see to read with suitable glasses for his myopia. The ataxy of the legs continued, and to it was gradually added loss of power, with spasticity of the limbs.

He remained in this state until 1904, when he began to develop signs of bulbar paralysis from pressure, and died of this from failure of respiration with filling of the lungs in September, 1904. Leave was obtained to examine the brain, but this could not be done until forty-eight hours after death. The cerebral convolutions were flattened, and the ventricles much distended and filled with cerebro-spinal fluid. Otherwise the cerebrum was normal. The cerebellum was very much softened, and was occupied by a large, firm tumour the size of a small apple; this was oval in shape, and involved the right lateral lobe chiefly and very extensively, but also extended into the middle and left lateral lobes. From the condition of the parts the exact origin and relations of the growth could not be determined. The pons and medulla were flattened from pressure. The growth proved on microscopic examination to be a fibroma.

Thomas J., æt. 50. This patient was first seen in September, 1896, when he stated that he had enjoyed good health until two years previously. He had been quite temperate for twelve years. He had never before this illness suffered from headache, deafness, nor ear-discharge. The onset began with " a cold " two years previously, when he became absolutely deaf in the left ear; shortly afterwards his hearing began to fail in the right ear, until now he can only occasionally hear when one shouts loudly into his right ear. Soon after the deafness appeared he began to suffer very much from tinnitus aurium and giddiness. Twelve months previously his gait became staggering, " like a drunken man," and this was much worse in the dark. About this time he had a sort of epileptiform fit.

On admission he complained much of deafness and tinnitus aurium; mentally he was quite sound. Pupils equal; act well to light and accommodation. Slight nystagmus in all positions of the eyeballs, most marked in the horizontal. No cranial nerve-palsy. Speech normal. No optic neuritis. Knee-jerks were increased. There was no ankle-clonus. There was a marked " cerebellar " gait, and Romberg's symptom was present. He was treated with hypodermic injections of pilocarpine without benefit.

He left the hospital, and was seen next in May, 1898. In addition to the other symptoms, he had now dragged his left foot for over one year, and consequently had difficulty in going upstairs. Giddiness, tinnitus, deafness, and unsteadiness of gait were unchanged. He had especial difficulty in turning. Although he said the left knee felt the weaker, and inclined to give way, he tended to walk and to fall towards the right; on closing his eyes he fell backwards at once. There was some rigidity in the leg, with slight ankle-clonus; both knee-jerks were now much exaggerated, the left most. Plantar reflexes active. Double optic neuritis was present, most marked in the right eye. Slight horizontal nystagmus was seen. No cranial nerve-palsy. There was left hemianæsthesia, especially to pain, less marked over the face and head than over the body and limbs. Otherwise sensation normal. Intelligence good; he understood what was said to him by reading the movements of the speaker's lips. He complained of severe frontal headache.

In August, 1898, the staggering character of the gait and the tendency to fall to the right had increased. There was marked ataxy of movement in the left arm and hand, and, in addition and distinct from inco-ordination, a tremor of moderate amplitude, which was decidedly increased on voluntary movement. The deep reflexes were now also exaggerated in the left upper extremity.

During September and October his condition varied, but on the whole tended to become worse. The gait was now, owing to the rigidity, which was, however, never extreme, and weakness of the left leg, a compound between a cerebellar and an hemiplegic gait, and he had increasing difficulty in getting about. He had more headache, and was becoming more emotional. The optic neuritis remained at about the same intensity. The right pupil was larger than the left. The nystagmus and other symptoms were about the same.

I lost sight of this patient subsequently, and have not been able to trace him. I think, however, that the similarity in the symptoms and the course of the illness in his case makes it almost certain that he was suffering from a similar lesion to that in the first case. Both cases show the importance of bearing in mind the occurrence of deafness and tinnitus as occasional early signs of a cerebellar tumour. Fortunately, in the majority of cases of tumour in this situation we are aided by the presence of optic neuritis, which, as a rule, appears early, and soon becomes intense.

There is one other situation in which a tumour may cause complete deafness, and that is when it grows in the corpora quadrigemina ; indeed, it is stated [2] that the immediate cause of deafness due to a cerebellar growth may be pressure upon the posterior corpora quadrigemina and internal geniculate bodies, through which the central auditory tract ascends.

The symptoms and course of illness in both these patients and the histological characters of the growth in Case I correspond to the description given by Fraenkel, Hunt, Woolsey, and Elsberg [3] of neuro-fibromata of the auditory nerve. It was unfortunate that in the latter case the condition of the parts was not sufficiently good to enable the exact origin of the tumour to be ascertained. The authors consider that these growths give rise to certain symptoms in order, and run such a course that they can be thereby distinguished from other tumours of the cerebellum or in the posterior fossa. These characters are:—

1. The long duration of symptoms, three to six years; whilst the *average* duration of all cerebellar tumours is two years.

2. The initial and most striking or special symptoms, namely, tinnitus aurium, Ménière's syndrome, and deafness, are referable to the auditory nerve, and are of long-standing and gradual onset.

3. The general and focal symptoms are those present in any tumour of the posterior fossa, and come on gradually in the course of the illness, the former comprising headache, vertigo, vomiting, and optic neuritis; and the latter cerebellar ataxia, homolateral or crossed paralysis of the extremities, paralysis of the cranial nerves (especially of the seventh, sixth, and fifth), nystagmus, dysarthria, dysphagia, and paralysis of the conjugate movements of the eyes.

With this description the two cases given above fairly correspond, the peculiar points being the long course, the complete deafness, with tinnitus aurium, and the appearance of these symptoms at the onset, to be followed, after a considerable interval of time, by others characteristic of cerebellar disease. The successful result of the craniotomy in the first case is also worthy of remark. The patient was relieved of headache, and the optic neuritis subsided; so that he preserved his sight to the extent that he could read quite small print, and lived in comparative comfort for more than four years after the operation.

Attacks of auditory vertigo, or the set of symptoms known as Ménière's syndrome, are well known to occasionally occur in cases of cerebellar tumour. They may or may not be associated with deafness, and consist of severe attacks of vertigo, with tinnitus, ending in vomiting. If, as sometimes happens, these attacks are the first signs of a cerebellar tumour, preceding, as they sometimes do, all other symptoms for some little time, they may lead to a mistaken diagnosis of labyrinthine disease. Fortunately, as said above, optic neuritis occurs early in the majority of cases of cerebellar growths, and its presence would of course show that the condition present was not merely due to disease of the internal ear.

In a man, aged 45, the first symptoms of illness consisted of violent attacks of giddiness, in which he had to lie down to avoid falling, ending in vomiting, faintness, and palpitation. There was no deafness at first, and very little tinnitus. For some months these were the only symptoms, except that there was slight optic neuritis, most marked in the right eye. The presence of this optic neuritis gave the clue to the right diagnosis; without it the attacks would have been attributed to auditory vertigo. Later a staggering gait, weakness of limbs, deafness, intense optic neuritis, vomiting, headache, and mental weakness appeared, and he died about 18 months after the first onset of symptoms.

*Post-mortem.*—A large fibroma was found in the left lateral lobe of cerebellum.

Optic neuritis, from its usually early occurrence so valuable in diagnosis, may, however, be absent even in large tumours of the cerebellum. Unless the other symptoms are pronounced, its absence may render the diagnosis of the nature of the cerebellar disease uncertain. Ferrier[4] states that optic neuritis was present in nine out of ten cases under his own observation, and in sixty-four which he analysed it was present in forty-six, absent in four, and not mentioned in fourteen.

In a case recently under my care optic neuritis was absent throughout, although the disease ran a very short course, only lasting five months from the first appearance of symptoms, and the tumour was a very large one. Moreover, there was a second growth in the frontal region of the cerebral hemisphere. The growth was a round-celled sarcoma, and contained large cysts. It has been stated that gliomata and sarcomata of the brain, which form cysts, are for some reason less likely to give rise to optic neuritis. The history of this patient is briefly as follows :—

He was a gardener, aged 44, and had always enjoyed good health until this illness. His father died of " cancer in the chest," his mother, aged 70, is weak-minded, and one sister is in an asylum for dementia. In September, 1904, he began to feel weak, and complained of numbness in the right foot, of weakness in the right arm, of attacks of vomiting, sometimes after meals, sometimes irrespective of them, and of giddiness, which had caused him to fall down several times, always towards the left side. Subsequently the giddiness increased, and was especially bad on movement ; he developed a marked staggering gait, and became feeble and uncertain on his legs. The deep reflexes were increased, the plantar were flexor in type. There was no oculomotor paralysis, the pupils reacted sluggishly, the optic discs were normal ; no deafness ; there was no affection of sensation or of muscular sense. He became drowsy, and took to his bed a fortnight before he died in a state of coma, which supervened gradually. During the last ten days of his life he lay coiled up in bed on his right side, and if moved from that position returned to it again.

*Post-mortem.*—A large soft sarcoma of loose structure was found to occupy the central portion of the middle lobe of the cerebellum, and to extend for a considerable way into each lateral lobe, replacing the greater part of the white matter. A cystic tumour, the size of a walnut, was also found in the frontal lobe at the posterior end of the first frontal convolution, and there were other tumours at the root of the right lung, and in the left supra-renal body.

The other symptom to which I wish to refer is tremor. The cerebellum is one part of the brain in which a tumour may give rise to a tremor of " intentional " character. This was so in the following case :—

Wm. B., aged 3 years. The illness began with sickness and diarrhœa, which lasted a week ; after this it was found that he could not stand, but was just able to hobble about by helping himself with his arms. The child screamed a great deal at times as if in much pain.

On admission he looked healthy and well nourished. The head was very large, measuring 22½ inches in circumference, the anterior fontanelle and the sutures for some distance from it were widely dilated. The child could not stand, and when set up in bed he tended to fall backwards. When lying down he could move his legs about freely, except that he had some difficulty in raising them off the bed. The deep reflexes were present, the superficial absent, except the plantar, which showed Babinski's sign. The pupils were dilated, and did not act to light or accommodation. There was no oculomotor paralysis, and when at rest the face appeared fairly symmetrical, but when he laughed or cried the right side of the face remained motionless, and the mouth was slightly drawn over to the left; the right side of the face was also but less noticeably paralysed for voluntary movements. There was a marked tremor of the arms and hands on movement, most evident on the right side, and this tremor was somewhat wide in range; when the limbs were lying at rest there was no tremor, but the least movement brought it out. The tremor closely resembled that of disseminated sclerosis in its "intentional" character. The child's speech was somewhat drawling; he was quite intelligent, and not deaf. There was very intense optic neuritis in both eyes.

During the further course of the illness the legs became rigid, and the deep reflexes were increased. There was no complete facial paralysis other than above described. The head gradually increased in size. The right upper extremity became very rigid, and he ceased to use it, grasping objects with his left hand only.

He lay on his back in a natural posture, but during the last two weeks of his life the arms were generally in a peculiar position, the right was rigidly adducted to the side, extended at the elbow and wrist with the fingers flexed, while the left was abducted, the forearm raised above the shoulder, and the fingers free. There was no rigidity in the left arm, and the tremor on movement continued throughout, but it was noticeable that as the rigidity increased in the right arm the tremor grew less marked and finally disappeared. He gradually became comatose and died.

*Post-mortem.*—There was a condition of pronounced hydrocephalus due to enormous distension of the ventricles. The grey and white matter of the hemispheres were greatly reduced in thickness. The cause of this distension was found to be a very large tumour growing from the under surface of the cerebellum, which had infiltrated the cerebellum, practically replacing the middle and extending into each lateral lobe. The pons and medulla were much flattened and thinned out from pressure. The structure of the growth was that of a glioma.

The interesting feature of this case, apart from its exceptionally rapid course, was the peculiar tremor, which resembled that of disseminate sclerosis, in being absent when the limb was at rest and supported, and becoming very evident on movement.

Tremors of this kind are sometimes found in tumour of the brain in three positions, most commonly when they occur in the region of the optic thalamus or in the mid-brain; less often when the growth is in the corpora quadrigemina or cerebellum. Other characters of the tremor are its increase on emotional or other psychical excitation, its absence during sleep, the affection of the upper extremity only, at any rate for a considerable time, and predominance in the upper extremity throughout. Further, as in this case, if spastic rigidity develops in the limb in the course of the illness, the tremor diminishes or disappears.

At first I thought from this symptom that the growth would be found in the optic thalamus in the case under consideration, especially as at first sight he appeared to have another peculiar symptom ascribed to growths in this situation, *i.e.* unilateral loss of emotional, not voluntary, facial movements. Later, however, it was seen, though the child's age made it difficult to determine, that both kinds of facial movements were affected, and the signs of cerebellar disease became clear.

In a former paper[5] I reported two cases in which this tremor was associated with tumours of the optic thalamus. In one of these there was degeneration in the superior peduncle of the cerebellum, and to a lesion of these structures, Professor Ferrier, from his experiments on monkeys, is inclined to refer the tremor in these cases.

In a recent paper[6] Dr. Gordon Holmes brings forward a large body of evidence to show that these tremors are particularly associated with lesions of the mid-brain, and that they are directly due to involvement of the nucleus ruber or of some part of the rubro-spinal system; that is to say, of the tract which by means of the superior cerebellar peduncle connects the opposite lobe of the cerebellum with the nucleus ruber, and by the rubro-spinal tract connects this nucleus, by fibres passing downwards, with the opposite side of the cord. The clinical symptoms of Dr. Gordon Holmes's cases, and the *post-mortem* results in those in which an autopsy was made, indicated involvement of either the superior cerebellar peduncle or the nucleus ruber. The anterior end of this nucleus projects, as he points out, within the usual anatomical limits of the thalamus, with which it has connections; so that it would be involved in growths of the posterior end of the thalamus of any size, and thus the relative frequency of the tremor in growths affecting the thalamus would be explained.

## REFERENCES.

[1] Allbutt's *System of Medicine*, vol. vii., 1899, p. 378.
[2] Dercum, quoted by Ferrier (*loc. cit.*).
[3] *Ann. Surg.*, 1904, xl. 293.
[4] *Loc. cit.*
[5] *Brit. M. J.*, 1891, i. 1,283; 1901, ii. 1,406.
[6] *Brain*, Autumn, 1904, xxvii. 327.

# ON RECURRENT MOTOR PARALYSIS IN MIGRAINE.

Recurrent paralyses in some of their varieties have recently attracted considerable attention.[1] In migraine an opportunity for observing such paralysis is very rare, for it is a commonplace that the symptoms in the great majority of attacks of migraine are exclusively on the sensory side. In what follows I propose to give an account of a family in which hemiplegia, with, as a rule, loss of speech, was a constant feature of attacks of migraine, and to such a degree as to be almost unique, so far as I can ascertain; and also to deal with the forms of motor paralysis which occasionally occur in this disorder.

The restriction of the attack to purely sensory phenomena is one of the most interesting features of migraine, and at the same time one of the most puzzling. In an affection like migraine, of which the exact cause is unknown, and in which there are no recognisable pathological changes, the diagnosis rests upon the symptoms and their grouping. As a rule, the peculiarity of the symptoms and the regularity of their order of occurrence make the affection as definite as any symptom-group in medicine. But in diseases where the diagnosis depends upon the symptoms it is essential that these should conform to the accepted type. This is especially the case when phenomena are present over and above those recognised as proper to the attack. In some cases of migraine which lie on the borderland between it and other neuroses the distinction is by no means easy, and sometimes must be left in doubt. Especially may such difficulty arise in deciding between a diagnosis of epilepsy and migraine.

In the family history given below the strongly hereditary character of migraine is well marked, and also the tendency to direct transmission of the disease. The characters of the attacks which mark them as belonging to migraine will, however, be better considered when the cases have been described.

Attacks of migraine may be associated with motor paralysis in several ways, excluding those cases in which it occurs in accidental association with independent organic brain disease, such as tumour, or in which it is doubtful whether atypical migraine does not belong to another affection such as epilepsy.

### 1. *Migraine Secondary to Structural Lesions.*

Attacks of migraine may be a symptom of onset in hemiplegia due to a vascular lesion or to an intracranial tumour. This group I do not propose to consider. In connection with the production of an attack of migraine by occlusion of an artery it may be recalled that Leonard Hill[2] produced an attack in himself by digital compression of one carotid artery.

### 2. *Long Standing Migraine Complicated by Paralysis.*

Cases in which migraine of long standing has issued in permanent paralysis, generally due to a vascular lesion. In some of these one of the phenomena of the aura of the attack, such as aphasia or hemianopia, has become permanent, but in others the permanent disability in no way corresponds to the aura. Instances of this kind are fairly numerous.

In a case reported by Oppenheim,[3] in a patient who suffered from old-standing migraine, there occurred in the course of an attack stupor with persistent aphasia and right hemiplegia, found to be due to thrombosis of the internal carotid at the origin of the Sylvian artery.

In Infeld's[4] case, a woman aged 27, who suffered from hereditary migraine, in one attack felt something give way in her head, and fell but did not lose consciousness. There resulted right hemiplegia, with hemianæsthesia and blindness of the right eye. One month later there remained weakness and spasticity, with post-hemiplegic disorder of movement and slight paræsthesia.

J. J. Thomas[5] gives two cases, in one of which an attack like migraine was followed by left hemiparesis, hemianæsthesia, and hemianopia; in the other, a woman aged 27, subject to migraine, left hemiparesis, hemiparæsthesia, and hemianopia resulted. In both cases hemianopia was permanent; the other symptoms cleared up. He gives another case of migraine in which permanent hemianopia resulted.

Indeed, hemianopia as a permanent result of migraine seems to be more common than paralysis, although both are fortunately rare. Often in these cases the hemianopia forms a very marked feature of the aura preceding the attack,[6] but this, as stated above, is by no means invariable. In one case under my care a woman, aged 35, had suffered for seventeen years with attacks of migraine preceded by right hemianopia. One morning she woke up with dimness of vision for objects to the right, and this in the course of a week developed into right hemianopia, which remained permanent. The optic disc looked pale, but was otherwise normal. Her vessels were healthy.

With regard to such cases as the above, those who believe that attacks of migraine are due to vasomotor spasm of cerebral vessels have raised the point whether constantly repeated spasm of an artery may not in time lead to disease of its walls, and hence to rupture or thrombosis. It is difficult to speak with certainty on this point, but the great infrequency of permanent paralysis in a disease so common as migraine, the fact (at any rate, in my experience) that sufferers from migraine do not suffer in greater proportion from atheroma or arterio-sclerosis than other persons not so affected, and the fact also that such paralysis when it occurs often affects persons under forty—the age of the patients mentioned above is noteworthy—are all against this view. There must, in addition to migraine, be some other factor at work. Further, as Spitzer[7] points out, if repeated vasomotor spasm led finally to thrombosis it would be expected that the finest arterial twigs would be affected, whereas in some of the recorded cases large vessels must have been involved. Exception to this last statement should be made for a few cases in which there was good evidence of thrombosis of the central artery of the retina.

J. J. Thomas[8] states the case very fairly by concluding that migraine may occasionally result in permanent paralysis, aphasia, or hemianopia, and that in most instances this is due to an attack favouring a vascular lesion in persons who already have disease of the vessels, but that in others the lesion may occur in young persons whose blood vessels are in all probability in a normal condition ; and that although great caution is necessary, before ascribing such paralyses to migraine, to exclude coincident and independent disease—for example, of the vessels—yet a few cases remain which justify the statements made by Charcot and others that the normally transient hemianopia or aphasia may become permanent.

### 3. *Migraine Attended by Temporary Paresis.*

Cases in which paresis or even paralysis, temporary and recurrent, is one of the regular phenomena of the attack. In the ordinary way this consists of slight motor weakness in the limbs, generally the arm, accompanying or following the sensory disturbance—for example, pins and needles, etc.—of transient duration, from a few minutes to half an hour, not of common occurrence, and, as a rule, only present in severe attacks. For instance, a patient of mine, who suffered from severe migraine, described a pricking sensation in the right arm, which then went numb, and she could not feel if touched upon it. With the numbness there came loss of power; she could "move it but not use it." The same feelings spread to the leg, so that "she could not walk" for a few minutes. The symptoms passed off in the same order, and were most severe in the arm. According to her statement the sense of position of the limbs was retained. In Dr. Liveing's classical work on migraine, p. 14, a good case of this kind is given. His general conclusion is that "in some few cases loss of sensibility is accompanied by a certain loss of motor power in some parts—in fact, a transient hemiplegia" (p. 87). He quotes some other cases where the temporary paralysis was marked; one of those from Dr. C. H. Parry, of Bath, is a good example, but in some of the others the diagnosis seems to be doubtful; one of them, for instance, was a case of Adams-Stokes disease.

Spitzer[9] refers to the occurrence, as an unusual feature of migraine, of transitory paresis, of monoplegia or hemiplegia, but gives references chiefly to "ophthalmic migraine." Féré describes a case in which paralysis and loss of sensation came on with attacks of migraine shortly after the onset of the attack. The paralysis lasted for one to one and a half hours and disappeared with the scotoma. Cases of transitory aphasia are not so uncommon as part of the attack; in most of the cases the speech affection is stated to be sensory aphasia, but in some it is due to defective articulation, the patients are not able to "form their words," whilst full comprehension is retained. Otherwise, I have not been able to find in the literature of recent years any cases of transient hemiplegia occurring during attacks of migraine and complete for the time they last, which are quite free from objection as not being possibly due to other morbid conditions, for example, a previous attack of syphilis, present at the same time.

A remarkable case is reported by Professor Osler, in which attacks of recurrent hemiplegia, migraine, and angioneurotic œdema were associated in the same patient, though not at the same time. I quote from the account given by Dr. A. E. Russell.[10]

"The patient, a medical man, aged 29, at the age of twelve years had an attack of right hemiplegia with aphasia which lasted seven or ten days. Within the year he had five or six further attacks of hemiplegia, each successive one less severe and not accompanied by aphasia, and from that date was subject to occasional attacks of numb, tingling sensation in the side. From the age of 26 he became subject to severe attacks of migraine. At 28 he had a sudden attack of pain and swelling in the feet, and at the same time began to suffer from soreness at the ends of the fingers. He had frequent attacks of angioneurotic œdema of the upper lip and outbreaks of urticaria associated with severe darting pains in the legs. He had one attack of abdominal colic with pain in the calves of his legs, and an outbreak of purpura and urticaria; later, he suffered from hæmaturia and albuminuria. Professor Osler considered that the recurring attacks of hemiplegia were probably associated with changes in the brain of essentially the same nature as those which subsequently occurred in the lip and skin—in other words, that an angio-neurotic œdema occurred in the brain substance."

### *History of a Family in which Migraine was Attended by Recurrent Hemiplegia.*

I will now give the history of the family which has recently come under my observation. They belong to the working class, and, as is well known, people of this status often lose sight of their relations, and are unable to give accurate details of their condition. The three members of the family from whom I obtained the information were above the average in intelligence, and clear in their statements. Evidence as to four generations was available. The great grandparents (H) were said to be free from the affection, and had a very large family (the exact number was not ascertained), of whom four certainly—one son and three daughters, and possibly another son—were affected. Two of the daughters were unmarried, the third married a man not liable to migraine and had a daughter, who had at least one attack of migraine with paralysis.

CASE 1.—The son, $H_2$, suffered from attacks of headache with transient paralysis all his life; the paralysis involved one side only, and there was marked affection of vision. His last attack occurred about the age of 54; he was taken in a tramcar with loss of power in the right arm and leg and great impairment of vision followed soon by intense headache. He had to be carried home from the car, as he could not walk without support. Pleurisy or pneumonia followed shortly after this attack, of which he died three weeks later.

The history of the affection of vision, hemiplegia, and headache which occurred in the tramcar in this order was very definite, and the other attacks from which he had previously suffered were stated to be similar, and equally severe as regards the loss of power.

This man had a son, $H_3$, a daughter (M), both affected, two other sons unaffected, and another daughter who at the age of 5 years had whooping-cough. After a violent paroxysm of cough she had right hemiplegia, which lasted three weeks, and then cleared up, together with loss of speech, from which she took a long time to recover.

CASE 2.—$H_3$, examined, but not seen in an attack. A small, pale man, a porter, aged about 47; no evidence of organic disease. Has suffered from attacks of hemiplegia with migraine since the age of 28. For years they came on about every two to three months, but of late years have been much less frequent, and he has had freedom from them for as much as two years. If at any time he was run down in health the attacks came much more frequently. Order of phenomena in the attack: (1) Dimness of vision in both eyes, no scintillating scotoma; (2) sometimes simultaneously with this a feeling of numbness or tickling starting in toes or feet, and spreading upwards; (3) loss of speech, consciousness being unaffected, "he can understand what is said to him, but cannot reply"; (4) hemiplegia, in which there is absolute loss of power on one side, and he cannot stand, together with slight loss of sensation on the affected side; (5) nausea, occasionally vomiting. The loss of power, of speech, and the nausea last for about an hour, and as they pass away, (6) intense and incapacitating headache comes on and lasts for one to two days. Although the hemiplegia is of short duration, he is generally laid up for two days by the attack, and often does not feel quite well for a week. The hemiplegia is nearly always right-sided; both sides of the body are never affected in the same attack; loss of speech accompanies the hemiplegia, whether the latter is on the right or left side.

This man married a healthy wife; of the four children, aged 17, 14, 12, and 9 years, two are affected.

Case 3.—H $_4$, daughter of above, aged 14. This patient looks healthy, and presents no signs of organic disease. The attacks began at the age of 7, and recurred every two or three months, but have ceased for the past year. They consist of (1) dimness of sight, (2) loss of speech, (3) right hemiplegia, (4) intense headache with vomiting, followed by (5) drowsiness. She may sleep or lie in a drowsy condition for two or three days after an attack. The hemiplegia is always right-sided; loss of consciousness or muscular twitchings have never occurred. The hemiplegia sometimes comes on with extraordinary suddenness, so that she had been taken with an attack when standing, and has suddenly fallen from giving way of the leg. In this case the hemiplegia lasts for a few hours, or even a day.

Case 4.—H $_5$, a boy, aged 9. An intelligent child, but has always been delicate, and goes to invalid school. As a small child he suffered from severe rickets, and in consequence had difficulty in walking until the age of 7 years. He then had an operation for straightening his legs, and after that was able to walk and improved in health. He has been well lately, and on examination, except for some anæmia and traces of rickets, there was no evidence of disease. He has had two attacks in which there was a greater extent of paralysis than in any of the other patients.

On October 25th, 1909, he was taken for a midday drive in the carriage belonging to the invalid school which he attended, and the lady in charge thought that he looked ill. The child then said to her: "Miss R——, it is getting dark. I can't see you." Shortly afterwards she lifted him out of the carriage, and found that he could not stand, and had lost the use of his right leg, loss of power in the right arm quickly followed, together with loss of speech; he seemed to know what was said to him, but could not answer; the face was not affected. Twenty minutes later he lost power in his left leg, and then in his left arm, so that he was helpless and paralysed all over; moreover, he could not hold his head up; if lifted, it dropped again to one side. This attack lasted about two hours, and the paralysis began to improve towards the end of this time; he complained of headache in the frontal and occipital regions, asked to go to bed, and vomited two or three times. There were no muscular twitchings or convulsions. The paralysis passed off in the order of onset. The attack left him weak for three or four days, especially in the right arm and leg, and then he recovered completely.

On November 26th he had a second attack, without assignable cause, whilst at school. It began at noon with loss of sight, followed by loss of power, first on the right, and then on the left side, as in the first attack. Speech was also lost, but he was quite sensible. When brought home at 4.30 p.m. he had recovered speech, but was quite helpless, the loss of power affecting both sides of the body. He complained of very severe headache, and vomited all the day. Recovery took place in about the same time.

He was admitted into the Bristol General Hospital and remained there for nine weeks. During this time he had no attack. Beyond some anæmia, which improved under treatment, he appeared healthy, active, and intelligent for his age. At Christmas time he was purposely allowed to eat indigestible and rich foods, and as he had a large appetite he took full advantage of this, but no attack resulted.

After being for a week on a diet of bread 6½ to 7 oz., butter ¾ oz., meat 3 oz., 1 egg, potatoes 2 oz., rice pudding 3 oz., milk 16 oz., with one orange or apple, the analysis of the urine made by Dr. Emrys-Roberts was as follows :—

Quantity in twenty-four hours, 515 c.cm. Specific gravity 1020, acid, no albumen, no sugar, no deposit. Urea, 2.5 per cent. Uric acid (Hopkin's method), 0.3757 grams. Creatinin (twenty-four hours) 1.455 grams (Johnson's method ; two estimations). Phosphates calculated as phosphoric acid 1.03 grams. Chlorides calculated as NaCl 5.66 grams.

CASE 5.—$M_1$, sister of Case 2 ($H_3$), a healthy-looking woman, about 35 years of age. Examination detected no disease of the nervous system or of thoracic or abdominal organs. In her case the attacks began in childhood, and continued at intervals of two to three months until her last pregnancy, two years ago, during which they were much more frequent, sometimes recurring two or three times in one week. Since then for the past fifteen months she has been free from them. There was never any recognisable cause, and they came on at no particular time of day.

The first symptom is visual ; apparently there is hemianopia of the upper halves of the visual fields, for she sees only the lower half of objects looked at. This gives her a warning to lie down, as the next symptom is hemiplegia, which sometimes comes on suddenly, as she states that if she were standing she would fall down. The affected limbs feel heavy, "like lead." The hemiplegia is generally right-sided, but occasionally left-sided ; it is accompanied by loss of speech, but not of comprehension ; the speech affection accompanies the hemiplegia, whether the latter is on the right or left side. The face is apparently not affected. She has a peculiar feeling of swelling or thickness on the same side of the tongue as the hemiplegia. There appears to be hemianæsthesia as well as hemiplegia, at any rate in some of the attacks, for on one occasion when tested by a pin-prick there was no sensation on the affected side. There is no deafness, and no affection of the sphincters. After about two hours vomiting with severe frontal headache (bilateral) comes on, and the paralysis after the first attack of vomiting begins to gradually pass off. The headache always came with the vomiting, and never preceded the other symptoms. The patient has five children; the eldest, 9 years old, is Case 6; the younger ones have so far had no attacks.

CASE 6.—$M_2$, a boy, aged 9, was admitted to the Bristol General Hospital on November 30th, 1909. He had had two previous attacks of migraine with transient right hemiplegia during the preceding six months, from which he had completely recovered. He had had no other illness, and was a healthy, intelligent boy. He was left-handed.

On the morning of November 30th the boy complained of not feeling well and of a headache, and stayed home from school. His mother did not see him again until the afternoon, when she found that he was paralysed in the right arm and leg, could not stand, and could not speak. He also vomited.

On admission the patient was very cold and somewhat collapsed. His temperature was 95°. There was no head retraction, no convulsions, or muscular twitchings. There was right hemiplegia complete; the paralysis was flaccid. There was paresis of the right side of the face, affecting the lower part most, as in the ordinary hemiplegic type; the tongue was protruded to the right. He spoke very indistinctly and with difficulty, and occasionally used wrong words. He recognised his mistakes and understood what one said to him. He had some difficulty in swallowing. The right knee-jerk was said to be absent on admission, but as he was only examined lying down this is doubtful; it was certainly present next day.

On the next day, December 1st, the temperature was 97.6°; respirations 20; pulse 80, regular; tension normal. There was still well-marked right hemiplegia with flaccidity and slight hemianæsthesia—that is, sensation to touch and prick distinctly less acute than on the left side. He was conscious of the position of the paralysed limbs. He was still dull and drowsy, complained of left-sided frontal headache, had difficulty in speaking, used words wrongly, spoke slowly and indistinctly, and had slight difficulty in swallowing; he could only take liquid foods.

*Reflexes.*—Elbow, supinator, knee, and ankle jerks present normal and equal on both sides; abdominal reflexes present cremasteric absent, plantar reflexes extensor.

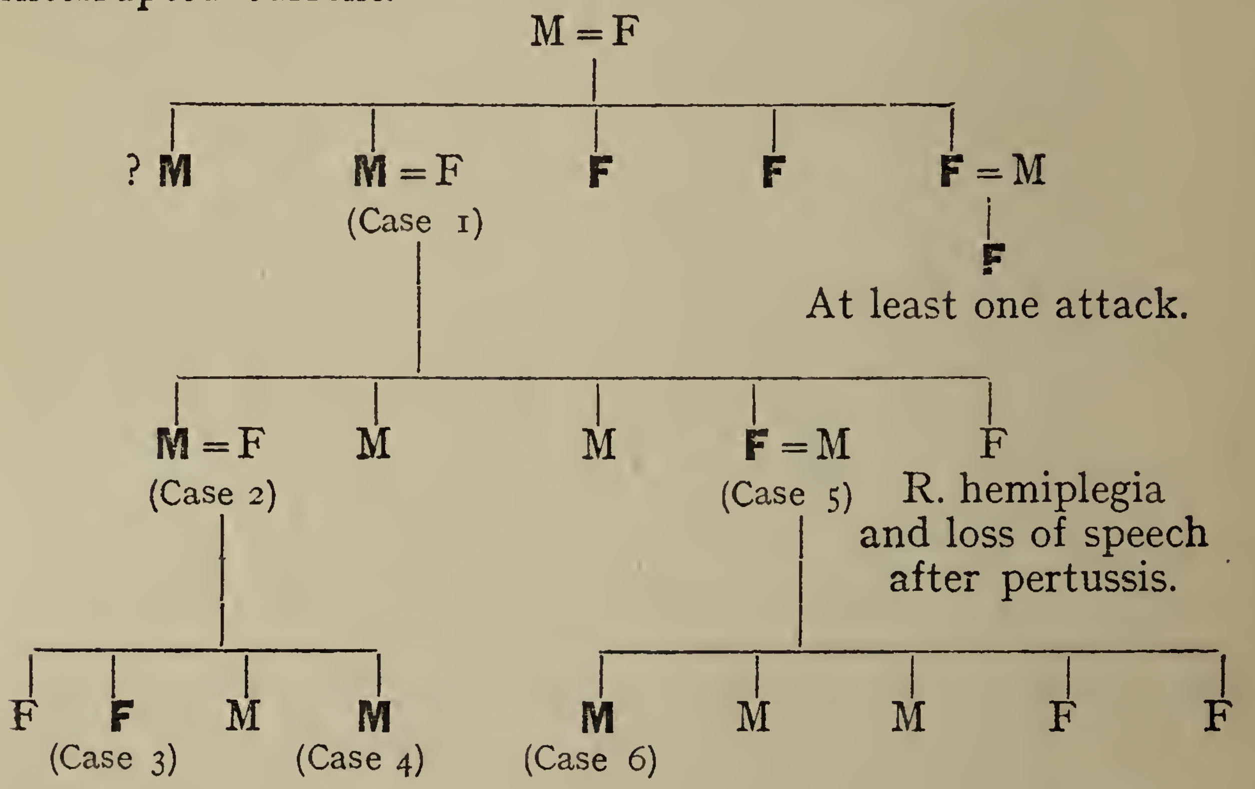
*Cranial Nerves.*—Well marked right hemianopia. Optic discs normal, except for some fulness of the veins. Smell normal.

No oculo-motor paralysis; no nystagmus; pupils equal, large, act to light and accommodation. Paresis of lower part of face on right side; orbicularis palpebrarum and frontalis muscles unaffected. Not deaf. Tongue protruded to right. Palate normal. No affection of sphincters.

On December 3rd there was still very slight defect of sensation to light touch, and prick on right side of face, front of chest and abdomen, and right arm and leg. No loss of sense of position of limbs. Paresis of right side of mouth and of right arm remained; the leg had recovered. There was no ataxy of movement. The reflexes as before, except that whilst the right plantar was of extensor type still, the left was flexor. He was still rather drowsy and speech was indistinct.

During the next two days the condition rapidly improved, and on December 5th he was normal, and there was no trace of paralysis left.

It may be added to the above that the motor loss was throughout much greater than the sensory, which was always slight; and that as this patient was the first member of the family to come under observation, and on admission we had no complete history with him, nor could he give any account of his two previous attacks, owing to the temporary loss of speech, the true nature of the condition was not at once recognised, and the electrical reactions were unfortunately not taken at the height of the paralysis. Later the muscles reacted well to interrupted current.



GENEALOGY OF A FAMILY WITH ATTACKS OF MIGRAINE WITH HEMIPLEGIA.

The first M and F had a numerous family (exact number uncertain), of whom four certainly, and probably five, were affected. The heavy type indicates the affected members.

Seeing that, as I have shown, motor paralysis to such a marked degree as existed in these patients is extremely rare in migraine, it is first necessary to establish the point that the attacks are of this nature. As there is no exact clinical test or pathologico-anatomical change to which we can appeal to make the diagnosis, each case must answer to certain criteria, which will naturally be those symptoms which are generally recognised as typical of the migraine attack. The more a case departs from the well-recognised type, or presents features not hitherto recognised as component parts of it, the greater care must be taken that the typical characters of migraine are present.

Attacks of headache more or less exactly reproducing the phenomena of migraine are occasionally seen as symptomatic of organic disease, such, for instance, as a cerebral tumour. Organic disease in these cases can be positively excluded by :—

1. The hereditary history.

2. Lapse of time in the older patients—the attacks have occurred for years—during which no sign of organic change has appeared.

3. The recurrent paralysis has not become permanent in any of them. In such severe attacks this of itself is remarkable, and is sufficient for the argument.

The following are the points on which I base the diagnosis of migraine for the actual attacks : (1) The marked hereditary tendency, direct transmission, and absence of other neuroses in the family ; (2) the onset of the affection in most of the patients in childhood ; (3) the characteristic visual phenomena preceding the headache, especially temporary hemianopia ; (4) headache, generally unilateral ; (5) the vomiting which generally accompanied the onset of the headache, and after which the condition of the patient began to improve ; (6) return to the normal in the interval between the attacks; and (7) the temporary loss of speech and sensory disturbance which are well-known features of some severe attacks of migraine. In all these points the attacks in this family so exactly correspond and these features so regularly repeat themselves in successive attacks—this regularity of repetition of the phenomena of the attack in the same patient being another characteristic of migraine—that the diagnosis of migraine seems to me established.

The remarkable feature is the addition of hemiplegia, or in one case of paralysis of all four limbs, and muscles of neck, which cannot be accounted for as a secondary result of the sensory disturbance present.

There are a few points in the attacks in this family worthy of further remark. First, the hemiplegia, loss of speech, and hemianopia were phenomena of the aura of the attack, and in all cases regularly preceded the headache. In most attacks in all the patients the hemiplegia was right-sided, and much less often occurred on the left side of the body. The speech defect was on the outgoing side of the cerebral mechanism for speech, the patients either could not articulate or only imperfectly, but could always understand what was said to them. This is contrary to what is described as the usual condition when aphasia occurs in migraine, for "sensory" aphasia is stated to be more common than "motor," although the latter occurs. Some of these patients were, however, definite on the point that they could hear and understand, and knew what they wanted to say, but could not speak. I think, generally speaking, that in migraine the affection of speech is not infrequently of this type.

This speech defect occurred indifferently with either right or left hemiplegia—that is to say, it regularly accompanied the hemiplegia, and in the adult patients, as well as in the children. In the latter it is well known that aphasia may accompany either right or left hemiplegia of organic origin. This indifference to the side of the hemiplegia seems to me a point of great interest. It has been observed before that in cases of migraine with sensory disturbance speech defect might accompany sensory phenomena in the left arm, left side of tongue, or left hemianopia.

The attacks seem to be becoming more severe as they descend the family, the two children last affected have more severe attacks than their parents, so much so that in one of them the paralysis affected the muscles of the trunk and limbs on both sides.

The frequently sudden onset of hemiplegia is particularly noticeable; more than one of the patients stated that if it came on when they were standing they had fallen down, and one used to lie down on the first appearance of the visual aura to avoid a fall. This is comparable with the sudden onset of hemianopia in some recorded cases of migraine. The relation of the attacks to pregnancy in Case 5 is curious, and it is well to accentuate the points that in none of the patients, even in case of a fall from sudden hemiplegia, was there ever a momentary loss of consciousness, or muscular twitchings, or convulsions, or affection of sphincters, or spasm of the muscles, the paralysis being of flaccid type.

Lastly, the recovery is complete between the attacks, and in no case have they left so far any permanent paralysis or disability.

In relation to the diagnosis of these cases reference must be made to the form of recurrent paralysis known as "family periodic paralysis." There can, I think, be no question as to the marked differences which distinguish the attacks of the latter disease from those of my patients. I have already given the points which identify them with an unusual and severe form of migraine, and need not recapitulate these further than to say that severe headache, hemianopia, and sensory disturbances—other than occasionally tingling and numbness—are not present in "family periodic paralysis," which consists of a recurrent and transient flaccid motor paralysis, not of cerebral type—for example, there is loss of electrical irritability in the affected muscles—affecting usually the trunk, all four limbs (proximal parts first), and muscles of the neck.

Whilst the attacks are thus distinct, there is another question as to a possible relation between the two affections. As a rule, migraine does not appear in the family history of the victims of family periodic paralysis, but in one remarkable family described by Holtzapple[11] the disease was closely associated with migraine. In four generations of this family eighteen persons suffered from severe attacks of migraine, and seventeen from periodic paralysis. Of the latter, five were subject to both affections, twelve to periodic paralysis only, and thirteen to headache only. All the patients were descended from an ancestress who suffered from sick headache only, and in the branch of the family most severely affected, in which three deaths occurred, the mother had migraine but no paralysis.

In some respects the family I have described above affords features which carry whatever relation there may be, if any, between the two diseases a stage further, for in it there is the very unusual addition to typical migraine of an extensive motor paralysis, with a closer hereditary transmission than is often seen in ordinary migraine, and in one of the patients last affected in the third generation the paralysis, in the attack, beginning as a hemiplegia rapidly spread to the opposite side and affected the neck muscles, so as to become general.

The character of the paralysis in the two affections is, however, so essentially different that any apparent connection may be no more than the common tendency for one neurosis to be associated with another in the same or different members of a family.

In family periodic paralysis the seat of the lesion is in the muscles or in the junctions of the lowest motor neurones with the muscle fibres, whilst in migraine the paralysis is of cerebral type. It is impossible not to be struck with the similarity of the hemiplegia, accompanied by a greater or less degree of anæsthesia, in the cases described above, to the hemiplegia of functional disease, especially hysteria. There are, however, differences between them which probably indicate in this case also a difference in the anatomical seat of the lesion. For instance, in hysteria the alteration of the visual field is not a hemianopia, but a concentric contraction; the face altogether escapes, the paralysis is "ideational," and due to the dissociation of the highest psychical centres from those next below. According to Campbell, associated with each of the known cortical centres there is a corresponding higher or psychical centre. He describes a psycho-motor, psycho-sensory, psycho-visual, and psycho-auditory centre in close relation to the motor, sensory, visual, and auditory centres seated in the præcentral, occipital (calcarine), and superior temporal gyri. Dr. McDougall,[12] in his paper on the mode of action of fatigue in the nervous system, incidentally suggests that in hysteria the supply of energy is insufficient to overcome the resistances of the highest levels of the brain and to keep open the connecting channels.

In the recurrent hemianopia, disorders of sensation, and occasional paralysis of migraine the anatomical position of the lesion must be below these levels. It is important to note that these disorders occur early in the attack, precede the severe pain, and therefore they cannot be explained on any theory of inhibition due to the intensity of the latter. Moreover, abortive attacks are known in which transient hemianopia, aphasia, etc., are the sole features.

In Dr. McDougall's paper, referred to above, he attributes the phenomena of fatigue or exhaustion to such an increased ratio of the resistance to the supply of nervous energy at command at the synapses or junctions of the neurones that nervous impulses can no longer pass through, and the connection between the neurones at the points of junction or synapses affected is interrupted. This increased resistance at the synapses may be induced by exhaustion or by accumulation of the waste products of activity.

It is reasonable to suppose that some endogenous or exogenous poisons may act in a similar way on the nervous system and produce paralysis by greatly increasing the resistance at certain synapses.

Without entering into a full discussion of the various theories of migraine, it seems to me that the disease may be best accounted for by the accumulation within the body of some self-manufactured poison, gradually accumulating until a periodical attack results, and showing a selective action on certain neurones, or rather upon their synapses, and possibly by becoming attached to their receptors preventing them from carrying out their functions. In view of the known selective action of various poisons upon special sets of neurones, there is nothing improbable in such a view of the localisation of symptoms which characterise most attacks of migraine.

Such a view has, to my mind, more in its favour than the theory which is perhaps most generally accepted at the present time—namely, that vasomotor disturbance or spasm of cerebral vessels is the cause of the attacks of migraine. It must be admitted, however, that the pathology of migraine remains obscure in spite of the many explanations that have been offered, and, indeed, to suppose that in ordinary attacks the action of the poison remains localised to cortical sensory structures, whilst in cases such as the family above described there is in addition a toxin able to act upon the kinæsthetic (motor) centres is but to state in other words a clinical observation and not to explain its essential nature.

4. There is still another form of motor paralysis associated with migraine—the so-called ophthalmic migraine (Charcot's "migraine ophthalmique"). I have left this to the last, as it is impossible to consider it fully in this paper, and its connection with migraine is denied by good observers. Thus, it has been called hemicrania with third nerve paralysis.[13] Undoubtedly cases grouped together under this head own different pathological causes. Most commonly the paralysis is confined to the third nerve on one side, but in other cases of a similar kind the fourth, fifth, and sixth (and occasionally the seventh) nerves may be also affected. The reasons why some authors have separated these cases from true migraine are that in many cases there is no aura, no heredity, the pains may last for weeks, and some degree of paralysis persists in the intervals. There are, however, other cases which satisfy all the above criteria for ordinary migraine, and in which there is a return to normal between the attacks.

Probably the accounts have been written from two distinct groups of cases: (1) Cases in which intermitting attacks of third nerve paralysis are preceded by attacks of headache corresponding in clinical aspect (including aura and heredity) to typical migraine, and do not end in permanent paralysis; (2) cases which show periodic exacerbations, but in which from the first, or early in the course of the disease, there is a certain amount of persistent weakness which ends in permanent paralysis.[14]

In the first set of cases we may probably go further and say with Senator and Bernhardt that there is no recognisable lesion, whilst in the second group the lesions that have been found in the few cases that have undergone pathological investigation are (1) tumours (Karplus and Thomsen) at the base of the brain involving the third nerve, (2) a mass of granulation tissue, and (3) syphilitic lesions in the same situation.

Cases of this nature, however, form a clinical group so distinct from ordinary migraine that they are better considered apart from it until more is known about them.

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# CEREBRO-SPINAL SYPHILIS.

[Before proceeding to the subject of my lecture, I wish to pay my meed of tribute to the memory of Edward Long Fox, in whose honour these lectures have been instituted. There will come a time when the lecturer of the day will not have known him personally, hence it is the more a pious charge on those who have had the advantage of his friendship to commemorate his virtues. For they know well that Edward Long Fox was a man held in especial honour and affection by his medical brethren in this city and neighbourhood. Honoured for his wide culture and knowledge of his profession, and beloved for his warmth of heart and kindness of disposition, there was no member of his profession to whom in case of need he was not always willing to lend a helping hand, either by wise advice or substantial aid. I myself am indebted to him on more than one occasion for valuable counsel. Throughout a long professional life he never flagged to the end in maintaining a keen interest in the scientific side of medicine and in its progress. At the same time he followed the best traditions of the profession—long may they flourish amongst us—in keeping in touch with the great matters of literature and knowledge, and he was a man of deep and genuine religious convictions.

In his professional work Edward Long Fox tended especially to the study of neurology, in which he always maintained the greatest interest, at which he was a life-long worker, and attained to eminence in it. Indeed, his book on the *Pathology of the Nervous Centres* marks him as a pioneer in the early days of the long series of pathological investigations which in our time have led to such fruitful results.

In choosing Cerebro-Spinal Syphilis as the subject of this lecture, I therefore feel that it is one in which he himself was greatly interested, and by which I may, in some humble measure, do honour to his memory.]

A fundamental fact in pathology is that there can be no accurate knowledge of a disease until the cause is known, nor can that knowledge be full and complete until the disease can be reproduced experimentally. The anatomical, coarse and microscopical, lesions of syphilis have long been known, and the treatment empirically determined. The constant and characteristic histological structure of syphilitic lesions pointed to a reaction on the part of the tissues of the invaded organism to a specific agent. The marked and peculiar infectivity of the disease further indicated the action of a living micro-organism. The rapid advance in bacteriological science, and the discovery that the lesions of tuberculosis, in which again characteristic histological tissue changes are constantly present, are due to a bacillus, naturally led, but fruitlessly, to the search for a bacillus in syphilis. It was from the first, however, recognised by most observers that the course of syphilitic affections was a peculiar one, and did not exactly correspond to that of any known bacterial disease.

In recent times three most important discoveries have been made, by which the study of syphilis has been enormously advanced, and features of the disease, which for centuries remained obscure and impossible of explanation, have been already largely elucidated. These three discoveries are (1) that of the spirochæta pallida or treponema pallidum by Schaudinn, and its establishment as the infective agent and cause of syphilis; (2) of certain specific reactions in the blood and cerebro-spinal fluid of the subjects of present or past syphilis, which have already proved of the greatest clinical value in diagnosis; and (3) the experimental communication of the disease to the higher apes.

There is little reason to doubt that the gap in the present knowledge of the life-history of the spirochæta pallida, that is the mode in which it exists outside the body, will shortly be discovered. When this step is accomplished there is equally little reason to doubt that more effective measures for prevention of the disease will be attained, and also further developments in the cure of syphilis in its early stages. The latter have, indeed, if the hopes based upon Ehrlich's new remedy are well-founded, already been successfully started.

The spirochæta pallida is present in all cases of syphilis, and is not found in any other disease. It has been found in every kind of syphilitic lesion, in the changes (reaction by tissues) provoked by the organisms. Mott states that Levaditi's experiments suggest that they stimulate the fixed tissue cells to proliferate, and then invading this bed of young cells, rich in nuclein, the organisms by the action of some secretion or in some other way cause these young cells to undergo lysis, thus providing the necessary pabulum for their own growth and multiplication. Probably these young cells are more easily attacked and destroyed than the older ones, and this may be the reason why the spirochætes are found in such numbers in the fœtal tissues in congenital syphilis.[1] From the seat of primary infection the spirochætes soon reach the nearest lymphatic glands, where they multiply in the sinuses and spaces, and then pass into the general lymph stream, infect distant glands, and by way of the thoracic duct may cause a general infection. The spirochætes have not been found in the cerebro-spinal fluid except in a few instances.[2] Hoffmann has, however, succeeded in inoculating an ape with syphilis with cerebro-spinal fluid obtained free from blood from a man with a papular syphilide.

It has been already stated that the course and manifestations of syphilis do not correspond with those of diseases produced by bacteria. Mott[3] has pointed out the great similarity of the histological lesions in the nervous tissues in chronic trypanosome infections, *e.g.* sleeping sickness, and dourine to syphilitic and parasyphilitic lesions. The universal perivascular infiltration in the central nervous system of lymphocytes and plasma cells, formerly thought to be pathognomonic of general paralysis and syphilis, he has shown to be equally characteristic of, and identical in, sleeping sickness, and gives the following points of resemblance and difference between sleeping sickness and syphilis.[4] They resemble one another in (1) early phenomena of infection; (2) a sore or other irritation at points of entry; (3) period of incubation; (4) invasion of local lymphatic glands leading to a general infection of the blood stream; (5) presence of erythematous rashes with constitutional disturbances due to migration of spirochætes into blood stream; (6) the occurrence of polyadenitis and lymphocytosis. Points of difference are:—

| SYPHILIS. | SLEEPING SICKNESS. |
|---|---|
| Invasion of nervous system in 5 to 10 per cent. only. When spirochætes invade subarachnoid space they remain within lymphatics, and do not become free in cerebro-spinal fluid. They are not found in blood, and multiply only in lymph-spaces and channels. | Chronic inflammatory affection of lymphatics of central nervous system.<br>Subarachnoid space always invaded and trypanosomes free in cerebro-spinal fluid, and usually in blood. |

Mott suggests that the extreme activity of the trypanosomes of sleeping sickness enables them to penetrate the walls of the capillaries, whilst the very slow and screw-like movements of the spirochæta pallida do not allow it to do so, and also that the deadly results of the *Trypanosoma gambiense* are due to the organism having acquired the power of passing into the subarachnoid space.

Passing over the second point, the communication experimentally of syphilis to the higher apes, the third discovery is that of Wassermann's and of other tests which in competent hands have already proved so valuable in diagnosis. For details as to these tests the reader may be referred to Mott's admirable Morison Lectures, from which I have already largely quoted. A few words may be said as to the nature of the test in syphilis, and first may be mentioned the fat-like substances known as lipoid bodies contained in all living cells, and probably essential to their vital activity. They consist of (1) nitrogen and phosphorus free bodies, cholesterol-fatty acids and lipochromes; (2) phosphorus free, but containing nitrogen, cerebrosides; (3) nitrogen and phosphorus containing phosphatides, lecithin, myelin. Monk[5] showed that the presence of lipoid droplets in a cell indicated dissolution of the nucleus and destruction of the cell, so that lipoid substances in great abundance indicate the breaking up of the nucleus, which contains much phosphorus, and the cell-protoplasm into lipoid substances.

Thus in diseases attended with the degeneration of neurones, *e.g.* tabes, general paralysis, thrombotic softening, etc., the destruction of the ganglion cells and neurones generally leads to the constant presence in the cerebro-spinal fluid of cytolytic products, lipoids, phosphatides and cholesterol, globulin and nucleo-protein. These products act as irritants, and excite a lymphocytosis in the cerebro-spinal fluid, cell-infiltrations, and changes in the ependyma of the ventricle. This lymphocytosis is most marked in the parasyphilitic affections in which also the above substances are found in greatest abundance. Although it has now been shown that the syphilitic virus induces metabolic changes, whereby larger amounts of lipoid substances are present in the serum and cerebro-spinal fluid in general paralysis and tabes than in other diseases, yet these substances also exist in normal serums, and the change is therefore rather a quantitative than a qualitative one.

Levaditi and Yamanouchi state that in Wassermann's reaction the use of extracts of liver as antigen depends on the presence of bile salts and (lecithin-containing) lipoids, and certain substances in the serum which are not syphilitic antibodies, but bind up with certain constituents of normal and syphilitic tissues. The serum reaction of syphilis and general paralysis is the same, and has no relation to spirochæta pallida, and is not due to the intervention of syphilitic antibody or antigen in the usual sense of these words.

They consider that Wassermann's reaction is due to the presence in the serum and cerebro-spinal fluid of unknown bodies, which may be cholesterol-esters, which precipitate and determine the fixation of the complement in presence of bile salts, soaps, lecithin, etc. Wassermann's reaction is caused by a histogenic and not a bacterial substance, and is quantitative and not qualitative.

These new views do not militate against the clinical importance of the test. Mott thinks it probable that the syphilitic virus brings about an increased loosening of the complex lipoids containing lecithin and cholesterin from the cells of the body and the red corpuscles of the blood throughout life. In tabes and general paralysis this affects the central nervous system, which normally is protected against the loss of its lipoid substances, and hence their presence in the cerebro-spinal fluid.

To conclude, Wassermann's reaction is positive in nearly all cases of syphilis, is a specific reaction, but does not indicate the organ affected. It may be obtained after twelve to fourteen days in primary syphilis. As it is a complicated process, difficult to carry out, efforts have been made to simplify it. The most promising modification seems to be Fleming's test.[6] This depends upon the fact that human serum is normally hæmolytic to the red corpuscles of the sheep. The three bodies required for this test are therefore the antigen (extract of liver or heart muscle), the suspected serum, and washed sheep's corpuscles.

Noguchi's test depends upon the presence of a globulin in the blood serum and cerebro-spinal fluid in syphilis. The slightest trace of blood in the latter renders it valueless for this test. This globulin has been identified with euglobulin. Noguchi states "that the high value in complement binding exhibited by blood serum from syphilitics and by spinal fluids from general paralysis is associated with an excessively high content of globulin, but there does not exist a direct quantitative relation between the two." [7]

We may now turn to the results obtained by the application of Wassermann's, Noguchi's and Fleming's tests in the diagnosis of cerebro-spinal syphilis and parasyphilitic affections. I am much indebted to Mr. Scott Williamson, Pathologist to the Bristol General Hospital, for kindly giving me the results of his researches into the comparative value of the different tests. Mr. Williamson considers that Wassermann's reaction with careful technique is a quantitative method, and that Noguchi's modification falls into the same category. A negative result from Fleming's and Sabrazé's methods always went with a negative Wassermann, but with positive result from the two former, seven cases failed to give a positive result by Wassermann used quantitatively. It would therefore seem that a negative Fleming or Sabrazé is more reliable than a positive.

Wassermann's and Fleming's reactions behave similarly under mercurial treatment. The reaction may disappear in a varying time—on an average five to thirteen months in Mr. Williamson's cases. It may not disappear under the most energetic administration of mercury.

The accompanying table gives the chief results.

Other tests of much value in syphilis and parasyphilis of the central nervous system are the presence of a lymphocytosis, and of globulins in the cerebro-spinal

## TABLE I.—WASSERMANN'S REACTION.

| | General Paralysis. | | | Tabes Dorsalis. | | | Cerebro-Spinal Syphilis. | | |
|---|---|---|---|---|---|---|---|---|---|
| | No. of Cases. | Serum. | C.S. Fluid. | No. of Cases. | Serum. | C.S. Fluid. | No. of Cases. | Serum. | C.S. Fluid. |
| Boas .. .. .. .. .. | — | 94 %+ve | — | — | 78 %+ve | — | — | — | — |
| Ledermann, 1909 .. | 48 | 45+ve | — | 116 | 110+ve | — | 45 | 34+ve | — |
| *Ibid.*, 1910 .. | 23 | 20+ve | — | 68 | 52+ve | — | 27 | 24+ve | 3+ve |
| Plaut .. .. .. .. | 95 | 95+ve | 94% | — | — | 70–80% | — | — | — |
| Smith and Candler .. | 64 | 64+ve | 59+ve | — | — | — | — | — | — |
| Flashman and Butler .. | — | 98%+ve | — | — | — | — | — | — | — |
| Mott .. .. .. .. .. | 46 | 46+ve | 41+ve | — | — | 60% | — | — | — |
| Eichelberg .. .. .. | 110 | 97+ve | 93% | 49 | — | 27% | 18 | — | 7+ve |
| Nonne and Holzmann | otal Cases 295* | 100%+ve | almost 100% | — | 60–70% | nearly always – ve, or reaction feeble | | | — |

* Lymphocytosis and globulin reaction +ve in general paralysis and tabes, almost without exception, and seldom fail in cerebro-spinal syphilis.

## MR. SCOTT WILLIAMSON'S CASES.

| | Cases. | Wassermann. | Noguchi. | Fleming. | Sabrazé. |
|---|---|---|---|---|---|
| General Paralysis .. .. | 43 | ++ | ++ | | + |
| Tabes .. .. .. .. .. | 11 | 9 | 9 | 11 | 10 |
| Cerebro-Spinal Syphilis .. | 5 | + | + | + | + |
| Gumma Cerebri .. .. | 2 | + | + | + | + |
| Imbecility (C.S. fluid) .. | 13 | 11 | 11 | 13 | 13 |
| Syphilis .. .. .. .. | 37 | 34 | 34 | 37 | 37 |
| Optic Atrophy .. .. .. | 5 | + | + | + | + |

fluid. Lymphocytosis is most marked in parasyphilitic affections, namely tabes and general paralysis.

Nonne and Holzmann[8] conclude from a study of nearly 300 cases that (1) in tabes and general paralysis, lymphocytosis and globulin reaction are present almost without exception, including incipient cases. (2) Both only seldom fail in cerebro-spinal syphilis. (3) Their results with Wassermann's reaction are given in Table 1. They lay stress upon the constant presence of a marked reaction in the cerebro-spinal fluid of general paralysis, and its absence or feebleness in tabes as a distinction between the two diseases. (4) If this test is positive in epilepsy or tumor cerebri, the epilepsy is a sign of cerebral syphilis, and the tumour is a syphilitic neoplasm, or the patient is suffering from syphilis of some other organ. (5) Lymphocytosis and the globulin reaction are not causally related to Wassermann's reaction in the cerebro-spinal fluid. In syphilitic disease of the nervous system all four reactions, *e.g.* lymphocytosis, globulin-reaction, and Wassermann's reaction for serum and cerebro-spinal fluid, are in their intensity and relation to each other independent of the stage and course of the disease.

Eichelberg states that there is no regular correspondence between the Wassermann and globulin reactions. The latter is more often positive than the former in early cases of general paralysis, tabes and cerebro-spinal syphilis.

Further points made by various observers are that the Wassermann reaction is never positive in the cerebro-spinal fluid unless it is positive for the serum, that a negative result in the serum renders general paralysis unlikely, and that in syphilitic patients with positive serum reaction and a normal central nervous system the cerebro-spinal fluid is negative. The test is as a rule negative for the cerebro-spinal fluid in cases of cerebro-spinal syphilis where the serum is positive. A positive Wassermann reaction does not necessarily accompany an excess of lymphocytes. In initial and stationary cases of general paralysis and in old cases of tabes a positive result is not obtained so constantly in the cerebro-spinal fluid as in the serum. Zaloziecki holds that in a very early stage of general paralysis a negative result does not absolutely exclude the disease, and Jackowski and Rajchmann state that remissions in this disease correspond to a more or less complete disappearance of the reaction.

The effect of mercurial treatment in cerebro-spinal syphilis is to abolish the reaction after a varying time; it may again, however, become positive. Treatment by inunction and by injections of mercury is more effectual in this respect than by the mouth. Treatment is also more effective in recent cases of syphilitic infection.

Lastly, the reaction may throw light on the causation of cases not otherwise recognised as syphilitic. Thus Ledermann[9] in twenty-three cases of apoplexy found that in ten with a history of syphilis, six, and in thirteen with no such history, three gave a positive reaction; in twelve cases of aortic aneurysm the reaction was positive in ten; and the same result was obtained in fifty per cent. of cases of arteriosclerosis,—the last, if confirmed by other workers, a suggestive result.

In the action of the syphilitic virus on the central nervous system two very different effects are to be distinguished from the outset. Perhaps the most striking characteristic of the nervous system is the extreme differentiation in function of its various parts. In connection with this differentiation the selective action of poisons of all kinds is a marked feature of toxic influences upon it. This effect of various poisons, *e.g.* that of diphtheria in producing paralysis of accommodation, is too well known to need recapitulation. In studying the effects of the syphilitic virus, such selective action is found to be confined to what are known as para- or meta-syphilitic affections. I hold with those who consider that tabes and general paralysis are the sequels of a previous syphilitic infection. These affections present examples of the selective action of poisons directly or remotely due to syphilis. There are (1) the Argyll-Robertson phenomenon, which does not belong to cerebro-spinal syphilis, but is a feature of parasyphilis; (2) the decay of certain fibres of the posterior or sensory nerve roots in tabes; (3) in general paralysis, the destruction of cortical neurones, etc.; (4) primary optic atrophy; (5) tabo-paralysis.

In cerebro-spinal syphilis, on the other hand, there is no evidence of any such selective action of poisons. Its results are due to the long-recognised anatomical lesions of syphilis in the meninges, vessels, and supporting framework of the central nervous system, and the changes in the nervous elements secondary to these, and produced by interference with their nutrition, and by compression from gummatous exudations and tumours. These anatomical changes are uniform in syphilis. At all stages there are exudations of small round cells, necrosis of some of them probably by the destructive action of spirochætes, endarteritis and organisation later of such fibroblasts as escape destruction into sclerosing tissue.

A feature in the course of syphilis that has hitherto not been explained, but which seems likely to be cleared up by modern investigation, is the occurrence of gummatous or vascular lesions long after the primary infection. After long years of apparent freedom a person may develop tertiary symptoms. Once infected, the patient may be liable to syphilitic manifestations during the rest of his life. Further, the syphilitic process may modify or impress its specific characters upon the reaction of the tissues to any subsequent injury. This question is especially important in syphilitic nervous diseases, because they so frequently occur at long intervals after primary infection.

The late occurrence of vascular lesions is not difficult to understand, for from its known action on the arteries syphilis should produce a slowly-advancing change in them, which would lead after a considerable interval of time to narrowing and ultimate thrombosis, and hence to hemiplegia or paraplegia. The mode of production of late gummata is more obscure, but an explanation may be found in the discovery of spirochætes in tertiary lesions. This has been a matter of considerable difficulty, and for some time they were not found, but in a few instances they have now been demonstrated in gummatous tumours, and in the lesions of syphilitic aortitis. Moreover, though tertiary lesions are very rarely infective, Hoffmann succeeded in inoculating an ape from a gumma in a man 3½ years after infection. Hence it is possible that the spirochæte may remain long latent in the tissues and yet be potent for mischief. It is a common clinical experience that a gummatous lesion may arise at the seat of a blow or other injury. For this it would be necessary to suppose that the organisms must be widespread in the tissues for a chance injury to rouse them into local activity, of which evidence is lacking, and which seems, perhaps inherently improbable. Mott[10] suggests as possible explanations other than the above that the spirochætes have remained in some other tissue, *e.g.* the bones or spleen, and escaping thence, act by a kind of metastasis, or that there are forms of trypanosomes having a special affinity for particular tissues, of which there is a certain amount of evidence in the known instances of several cases of general paralysis following syphilitic infection from the same female; or again, the hypothesis above mentioned, that syphilitic infection so modifies tissue changes in the affected person that any inflammatory process shows itself in the peculiar form of the syphilitic lesion.

Passing on now to the clinical features of cerebro-spinal syphilis, we find that they depend on several pathological processes, which it is often difficult to differentiate from each other at the bedside. Briefly, they comprise disease of the vessels and the results of this, new formations or gummata, and inflammations of a specific or gummatous character, especially in the meninges. The symptoms of cerebro-spinal syphilis are not so often produced by one of these processes only, as by two or more occurring together in varying combination and relative intensity.

It is convenient to divide the cases into cerebral and spinal, and in some the disease so obviously affects either the brain or cord almost exclusively that this distinction is justified. However, even when such cases, in which symptoms referable either to brain or to cord dominated the clinical aspect, come to pathological investigation it is often found that all parts of the central nervous system are in some degree involved. Bearing in mind this fact, and also the difficulties of differential diagnosis between the several pathological processes, cases of cerebral syphilis may be further divided into those with (1) vascular lesions, (2) gummata, (3) meningitis only, and (4) those with vascular and meningeal lesions or gummata in combination. Especially in the last group both brain and spinal cord are affected together, and there is often a clinical combination at once suggestive of syphilis, a triplegia, a paralysis of one arm and both legs. Taking cases of triplegia first, the history of many is that the patient has had an attack of hemiplegia, due to syphilitic endarteritis, from which recovery has been more or less complete ; and then after a variable interval, in the majority about two to three years, but sometimes much longer, even twenty years, paraplegia develops ; or more commonly the hemiplegic leg has never completely recovered, and this disability increases together with the development of spastic paralysis in the leg hitherto unaffected. The type of paraplegia in these cases is generally spastic, with much rigidity and exaggeration of reflexes, but little affection of sensation. No doubt this condition may be due to a patch of thrombotic softening in the cord, or to a localised meningitis, but in some patients the signs are suggestive of a slowly spreading pyramidal tract degeneration. In view of the observations of Dr. Gordon Holmes and others, referred to later, the latter mode of origin, however, is open to question. The prognosis in these cases is bad ; I have only once seen a good recovery.

In considering cerebral syphilis, the space at my disposal will only allow me to refer to special points. In cases of cerebro-spinal syphilis some change in the mental processes is generally present, and too much stress can hardly be laid upon the diagnostic value of this. It is especially important amongst the prodromal signs, the patients often being apathetic, drowsy, forgetful, neglectful of work or duty, irritable or passionate. Of all prodromal signs the most frequent is headache, generally with nocturnal exacerbations. Of great importance are recurring paralyses, which are more frequently due to syphilis, especially in patients under forty-five years of age, than to any other cause. The occurrence of transitory aphasia, transient or permanent cranial nerve paralyses, and epileptiform fits in an adult not previously subject to epilepsy, should always suggest an inquiry as to previous syphilitic infection.

1. *In cerebral vascular syphilitic lesions* the early recognition of the nature of prodromal symptoms, amongst which recurring paralysis may be especially mentioned, is particularly important, in order that treatment may be instituted before the affected vessel is completely occluded ;

for, as has been often pointed out, once the vessel is closed, and necrosis in the area supplied by it has occurred, the result is the same, to whatever cause, syphilitic or other, the closure of the vessel is due. The common consequence of this form of cerebral syphilis is hemiplegia, with or without aphasia; syphilitic endarteritis in the retina is not uncommon, and is a valuable aid in diagnosis.

The most common cause of the hemiplegia is thrombosis. Dr. Head considers that hemorrhage is more frequent in cerebral syphilis than is generally held. The difficulty of distinction is, however, great. The final occlusion by a clot of a partly-obliterated vessel may be sudden, and before the final catastrophe the symptoms may not have been sufficient to bring the patient to the doctor. In two of the forty-eight cases of cerebral syphilis on which these remarks are based a diagnosis of hemorrhage appeared legitimate. The onset was apoplectiform with deep coma, and the resulting lesion was a hemiplegia of the ordinary type.

In the diagnosis of such cases from those of simple apoplexy the Wassermann test, the investigation of the cerebro-spinal fluid for lymphocytosis and a globulin reaction are of value. Although in such cases the prognosis as to recovery would hardly differ from that of simple apoplexy, prompt institution of anti-syphilitic treatment is important to prevent extension of the disease to other vessels.

Of what value these reactions may be the following instance shows.

A coachman, aged 37, was admitted with the history that seven days before he was taken ill with a high temperature and aching pains in the limbs; at the same time he spoke oddly, and left out words in talking. Two days later he became completely aphasic, and lost the use of his right arm. Seven months before this he had been thrown out in a carriage accident and cut his head; shortly afterwards he had total paralysis of the right third nerve, which passed off after some time.

On admission the right arm, right side of face, and right half of tongue were paralysed. The deep reflexes were exaggerated, and the abdominal absent on the right side. The pupils were unequal, but reacted to light and accommodation. He could only say a few monosyllables, used "yes" and "no" indifferently in reply to questions, had difficulty in repeating words said to him, and also in understanding simple sentences, *e.g.* he did not always correctly carry out simple movements when ordered to do so. He did not speak spontaneously. He could read aloud to a small extent, short words only, and then often substituted wrong ones, and did not understand what he was reading. Under these circumstances it was impossible to get an accurate medical history from him, but so far as could be understood he positively denied any venereal affection. Examination of the cerebro-spinal fluid, however, showed the presence of a decided lymphocytosis, and Noguchi's test was positive.

On this account active treatment with mercurial inunctions and iodide of potassium was begun without delay. He made rapid improvement: the arm began to recover first, then the speech very slowly, but it was three weeks before he began to attempt spontaneous speech.

In the sequel he was able to return home in six weeks' time, having recovered the use of his arm. He was able to write a letter, could read the newspaper and understand what he read, would reply to questions correctly, and to a certain extent spontaneous speech, though imperfect, had now returned. Before he left he told us that he had contracted syphilis at the age of twenty. The prompt institution of treatment was no doubt largely incidental to his recovery.

2. *Cerebral gummata.* As a gumma generally grows into the brain from the meninges it will first invade the cortex, and it is often therefore associated with Jacksonian and sometimes with general epileptiform attacks. It is rarely possible to diagnose a gumma as an isolated lesion, and *post-mortem* cases generally show concomitant meningitis or vascular disease. In some instances, however, clinical symptoms point to a gumma as an isolated lesion, and pathological investigation confirms this. Such gummata may occur in the substance of the cerebrum, cerebellum, or, as in one of my cases, in the medulla oblongata. The signs will then be those of a cerebral tumour; optic neuritis is not invariable, but is generally present, and is sometimes

intense. Should the gumma be in a position to cause hemiplegia this will be like that produced by other tumours, gradual in incidence, and of longer duration than that produced by vascular lesions.

Perhaps this is the place to put in a word against the administration of large doses of potassium iodide indiscriminately in all cases of intra-cranial tumour on the chance of their being syphilitic. Now that the tests mentioned above are available for diagnosis, such treatment is, to my mind, neither scientific nor justifiable. The condition of the patient deteriorates under the treatment, and valuable time is lost in deciding on the only real means of relief—operation—which all recent experience shows must be carried out early if it is to be successful in cases of cerebral tumours. A possible exception is, if the diagnosis can be made, that of inoperable sarcoma, in which, as in sarcoma of other parts of the body, large doses of potassium iodide may diminish the rate of growth of the tumour, or even check it for a time, but even here the best procedure would be a decompression operation.

In three of my cases it was possible to make the diagnosis of an isolated gumma. One of them died two days after admission, and the sole lesion was a large gumma of old standing in the left frontal lobe, which, if the patient had not been moribund on admission, could have been removed by operation. The other two made a very fair recovery under mercurial inunctions.

3. In cerebral *meningitis* there is a well-marked division of cases according to the affection of the base, convexity of the brain, or the membranes generally. In the two latter forms mental symptoms are as a rule present, and in about half the cases are pronounced, forming a marked clinical feature. The prognosis as to recovery has not seemed to me to be so good as in basic meningitis. In gummatous

basic meningitis paralysis of the cranial nerves is the characteristic feature ; the subacute ophthalmoplegias belong here, and paralysis of one side of the tongue, palate and one vocal cord is a well-known combination. The tongue is sometimes affected alone, showing hemiatrophy. When the disease affects the convexity, tenderness of the skull, either localised or general, is often present, headache is most intense and persistent, and there may be syphilitic disease of the bones of the cranial vault. In the following case an operation was undertaken for the relief of pain and of blindness, due to optic neuritis, and it illustrates the difficulties likely to be met with, and the advantages to be obtained by operation, and also the improbability of a permanent cure.

Annie P., aged 38, single. Previous to 1904 she always enjoyed good health. No history of any syphilitic manifestation could be obtained. In 1904 she began to suffer from nocturnal attacks of intense headache and vomiting of cerebral type. These continued through 1905, and she was in the Hospital twice on that account. On the second occasion there was a large tender node on the skull above the right occipital protuberance, which disappeared almost entirely under treatment with mercury and iodide of potassium. One day early in 1905 she was suddenly taken with loss of vision and vertigo. Subsequently she had frequent attacks separately of (1) loss of vision for one to two minutes ; (2) vertigo, in which there was twitching of the left arm and leg muscles, but never loss of consciousness. At first she had diplopia, lasting a few weeks, and passing off. Her vision steadily deteriorated, first in the right eye. She was found by Mr. Walker to have intense optic neuritis. All these symptoms diminished for a time under specific treatment, but early in 1906 returned with greater intensity, and vision deteriorated in spite of active treatment, until on March 16th, 1906, she had barely perception of light. There had been again for some time a tender bony swelling, 2¼ inches above and in front of the right external occipital protuberance. She was dull and drowsy, with marked slow cerebration, and the optic neuritis had persisted or increased. Under these circumstances I asked Mr. Firth to trephine over the bony swelling, and on doing so he exposed a large patch of carious bone. Trephining was a matter of great difficulty, as the bone was 3¼ inches thick, and dense, like ivory ; a large area was eventually removed. The dura mater was adherent to the bone, and on incising it a diffuse granulation-like tissue was found invading the cortex, occupying the whole area exposed, and extending forwards under the cranium. As much as possible was removed and the wound closed. The patient made a good recovery. The effect of the operation was seen immediately. The headache and vomiting, previously persistent, ceased at once; the following day she recognised her brother, and could see the pictures on the wall, and in a week could tell the time by her watch. In a month's time she was able to return home, resume her house-work, go out alone, and to write but not read. She remained well until August, 1907—fifteen months—when the sight began to fail, and the headaches and vertiginous attacks to return. Vision was reduced to a small chink, due to secondary atrophy resulting from the neuritis. She gradually became almost entirely blind from this cause, with return of cerebral symptoms, and appearance of left hemiplegia, and I believe died about two years later.

The occurrence of meningitis soon after primary infection is of considerable importance. In one of my cases meningitis (brain), with marked mental symptoms and slight optic neuritis, came on in a man, aged 26, five months after the infection. In another the symptoms were spinal, and were unmistakably those of spinal meningitis; they appeared three months after the primary chancre. Mott[11] in opening the discussion on "Syphilis of the Nervous System," at the Neurological Section, gave two examples of this early meningitis, and quoted a case reported by Goldflam in which symptoms of meningitis appeared one month after the chancre, and also one observed by Boidin and Weil, in which infection took place in June and signs of meningitis appeared in August, and four days later the roseolous rash came out. Lumbar puncture showed a pure lymphocytosis, and other observers have noted a lymphocytosis in the cerebro-spinal fluid during the secondary period. Mott suggests that the modern conception of the roseolar rash as due to the escape of spirochætes from the cutaneous capillaries makes it possible that a similar affection of the meninges may occur, and further that in rare instances the spirochætes in the blood may affect the meninges before the skin. Both my cases made a speedy and complete recovery under mercurial inunction, and the same result was obtained in the other cases mentioned above.

With regard to the group of cases in which the signs indicate co-existent vascular and meningeal lesions (gummatous meningitis), like the cases of triplegia mentioned above, evidence of vascular disease in the shape of an attack of hemiplegia not infrequently precedes the more general symptoms by two or three years. Apart from these preceding attacks of hemiplegia the onset is gradual in all. Optic neuritis is present in a few, and syphilitic disease of the retinal vessels is sometimes found, as in the cases of uncomplicated vascular lesions. Symptoms of mental disease are more pronounced than in any other form of cerebral syphilis, and occasionally end in syphilitic dementia, so that the patient has to be removed to an asylum. When mental symptoms are predominant in the case, they do not appear to be associated with predominance of any one form of lesion especially. The prognosis is in my experience bad. No case completely recovered, and improvement only took place to a limited extent.

There may be difficulty in diagnosis from general paralysis, but expansive ideas and delusions are generally absent, the mental changes are associated with various sensory or motor paralyses, hemiplegia, aphasia, cranial nerve palsies, etc. The Argyll-Robertson phenomenon is not present. The cerebro-spinal fluid shows a less-marked lymphocytosis than in general paralyses, and as a rule does not give the Wassermann reaction. Lastly, there is a varying degree of recovery under treatment. However, Turner points out that some cases which apparently begin as cerebral syphilis end as general paresis.

Turning now to some special symptoms of cerebral syphilis, out of forty-five cases *optic neuritis* occurred in nine, and in seven of these there were signs of meningitis with or without other lesions. In four cases, with diffuse cerebral lesions, optic atrophy was found either in one or both eyes. *Epileptiform fits,* indistinguishable from the attacks of general epilepsy, occurred in seven cases, in two being associated with localised fits (Jacksonian epilepsy). In two cases fits were the first, and for some time the only, sign of cerebral syphilis, and in three more constituted the most serious and prominent symptom. They were not present in any of my cases of spinal syphilis. The fits were of the major type, one patient only had attacks of *petit mal.* I bring forward these facts because syphilis has been held to be a doubtful cause of epileptic attacks. Recent observations go to show, however, that epileptiform attacks which cannot be clinically distinguished from those of idiopathic epilepsy occur for which no other cause than syphilis can be assigned. Cerebral syphilis is of course a well-known cause of Jacksonian epilepsy.

Dr. Head,[12] in the discussion already alluded to, referred to the occurrence of convulsions and epileptiform attacks in the early stages of syphilis, and Dr. Wilfred Harris mentioned three cases of syphilitic epilepsy arising without any apparent cause, in which there was a strong probability that the lesion was a diffuse meningitis. Certainly in epilepsy starting in adult life syphilis should be remembered as a possible cause, and in case of doubt a Wassermann's test carried out. Unfortunately the results of treatment are often disappointing, the fits tending to persist.

I have dealt with the question of the occurrence of the Argyll-Robertson phenomenon elsewhere,[13] and shall not say more than that in its fully-developed form, not a mere sluggish reaction of the pupils, I do not believe that it occurs in cerebro-spinal syphilis, but that its presence is an indication of a further degenerative change in the central nervous system, that is, of parasyphilis. Thus in any case in which it is found it must arouse fear of tabes or general paralysis, or possibly of some other degenerative (parasyphilitic) affection in the future, if signs of such disease are not already manifest. In sixty-seven cases of cerebral and spinal syphilis this sign was present in four cases, of which one developed tabes later, a second was possibly a general paralytic, the third had Erb's syphilitic spastic paraplegia, and in the fourth the sign present at first cleared up under treatment. In six the reaction to light was distinctly present but sluggish, and in three of these also improved by treatment.

A few further points may be added as to the prognosis in cerebral syphilis. In purely vascular lesions, even if treated early, the prognosis is not good, and as we have seen, hemiplegia of vascular origin may be followed a few years later by diffuse vascular and meningeal lesions; hence the very great importance of thorough treatment, and of seeing that the patient returns for fresh courses of treatment, although keeping well, at suitable intervals. In cases of isolated gumma and of pure meningitis the prognosis is fairly good, and there seems less tendency to a recurrence of fresh lesions. Rumpf considers that if the cranial vault is affected the result is likely to be unfavourable. Naunyn's[14] tables state that there is no material difference in percentage of cured and uncured cases, whether considered from the point of view of age at onset of symptoms, or whether they occur within a short interval or over ten years after infection.

Generally speaking, the ultimate prognosis when the symptoms indicate extensive lesions is not good. Although the immediate results of treatment are often very satisfactory, yet there is a strong tendency to the return of the trouble in the same or other forms of lesion, with the final result of a decided and permanent impairment of the patient's mental and physical capacity. He is no longer the same man in his business or profession, which he now carries on with less energy and ability, or too often is unable to carry on at all. Further, in the majority of cases life is shortened.

### *Syphilitic Affections of the Spinal Cord.*

In syphilitic affections of the spinal cord the symptoms in many cases are not solely confined to it ; thus there may be a transitory or permanent paralysis of a cranial nerve, especially of the third nerve, as for instance a temporary diplopia. Other signs indicating a general affection of the nervous system may occur, and perhaps be obscured by the predominance of the spinal symptoms. Thus some change in mentality, such as apathy, forgetfulness, or some confusion of ideas may be present and form an important factor in the elucidation of an obscure case.

The spinal symptoms themselves have often a somewhat bizarre character, and do not correspond with well-defined disease of the systems of neurones in the cord. The state of the reflexes may be contradictory, perhaps absent on one side or in one segment of a limb and exaggerated on the opposite side or in other segments. The presence of symptoms of mixed origin at different levels of the cord, indicating a widespread extent of disease and suggesting a variety in the pathological lesions, is of itself of diagnostic value. This wide extent and variety in the nature of the lesions has been laid stress upon by many observers.

Speaking generally, the chief symptoms are spastic paresis or paralysis with some ataxy, exaggeration of the deep reflexes, often to a marked degree, early affection of the bladder, and root lesions.

Of pure meningitis there was one example, in twenty-one cases analysed for this lecture, and that one, which occurred three months after infection, has been described above. A passing mention may be made here of the condition of chronic localised meningitis of the cord with a local collection of the cerebro-spinal fluid, occurring generally in the lower dorsal region, and giving rise to symptoms which resemble those of an extra-medullary tumour. This condition is sometimes the result of syphilis.[15] I have once seen an instance of an isolated gumma of the cord (not included in the present series). It was not diagnosed during life. The patient died of a syphilitic visceral disease. The signs of this rare condition would be those of a tumour of the cord.

The most common condition in cases of spinal syphilis is that generally entitled meningo-myelitis. This term is, however, not a very exact one, for in the majority there seems to be no inflammation of the cord itself, but compression of its circumferential zone from meningeal exudation, and patches of softening due to vascular thrombosis. Out of a large number of pathological observations, Gordon Holmes[16] found only one case in which there was a true myelitis. The usual changes were a diffuse meningitis or thickening of the soft membranes of the cord, in varying degree at different levels, with infiltration of round cells around the vessels. The cord itself suffers from compression and interference with its blood supply, but is not actually invaded by the disease. In addition there are peri- and endo-arteritis of the meningeal and intra-spinal vessels, and local patches of softening arise from thrombosis of them. The tracts in the cord most affected were the spino-cerebellar, direct cerebellar, and Gower's tract, hence the ataxy that so often accompanies syphilitic spastic paraplegia : the dorsal columns escape to a remarkable degree. He also emphasises the fact that such changes generally occur throughout the nervous system, and are not confined to the cord.

In my experience the onset is acute, somewhat sudden, or gradual in about equal numbers. Dr. Head thinks that the prognosis is less favourable in cases of sudden onset, but so far as my cases go the result bore no distinct relation to the mode of onset. Incontinence of urine, and often of fæces, is a common and early symptom. Recovery to the extent of ability to return to full work occurs in only a small proportion ; in the rest it is partial only, which generally means that some degree of spastic paresis, with defective control over the bladder, remains.

The disturbances of sensation are, speaking generally, less than those of motion, and recovery from them earlier and more complete. Sensation of any kind is most often not completely lost, but only partially affected. I have found loss to heat and cold most marked and most frequent, next loss to pain (pin-prick), whilst tactile sensation, though often impaired, was not so completely affected. Signs pointing to a lesion of a particular nerve-root or roots are not infrequent, and are valuable in the differential diagnosis. The variable condition of the reflexes, and want of correspondence in the alterations on the two sides or in one limb, have been already alluded to as a diagnostic feature. Thus one knee-jerk may be normal and the other exaggerated, both limbs being paralysed or paretic, or the knee-jerks may be normal with double ankle-clonus, an extensor plantar reflex in one foot and flexor in the other.

The appended charts illustrate some of the sensory changes met with, and in the description the state of the reflexes is also given.

An incomplete or modified Brown-Séquard syndrome may be present, and this also occurs in the rare cases of an isolated gumma in the substance of the cord. In this incomplete form this syndrome is more often found in syphilitic than in any other spinal-cord disease, but in its fully-developed form is not often seen. Dr. Wilfred Harris points out that

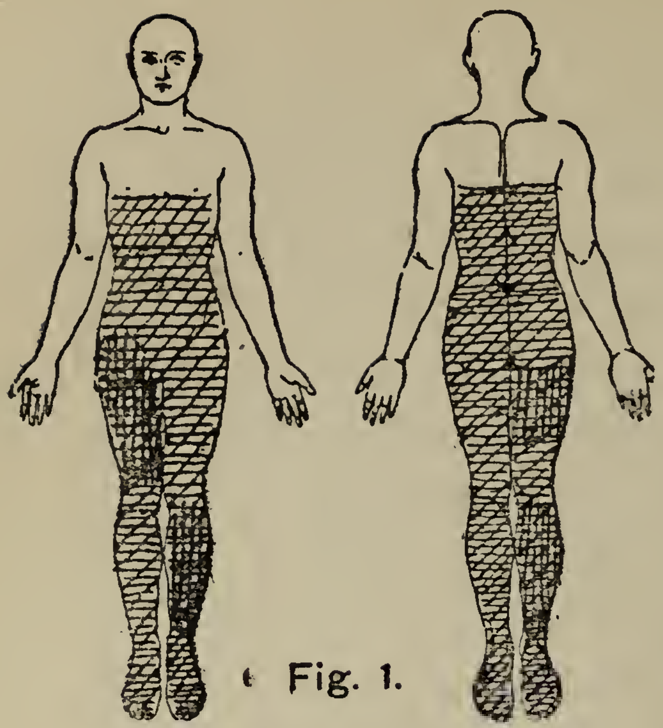

Fig. 1.

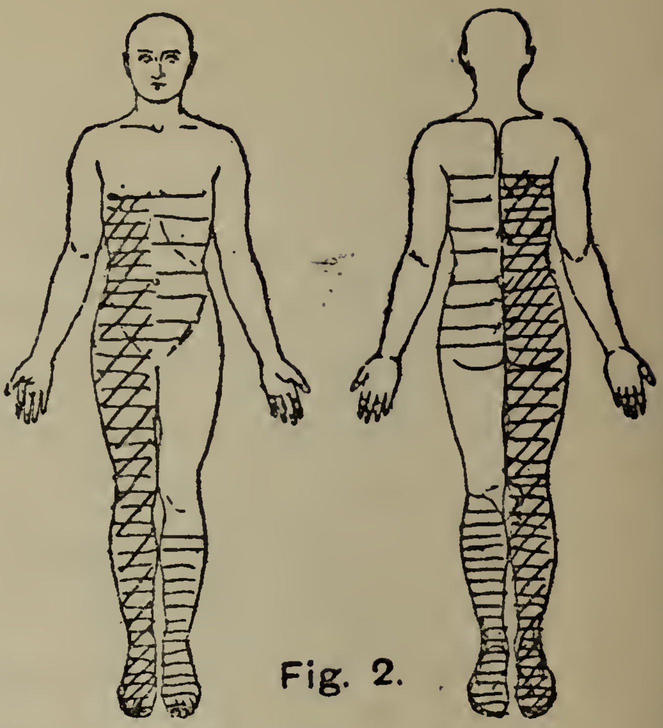

Fig. 2.

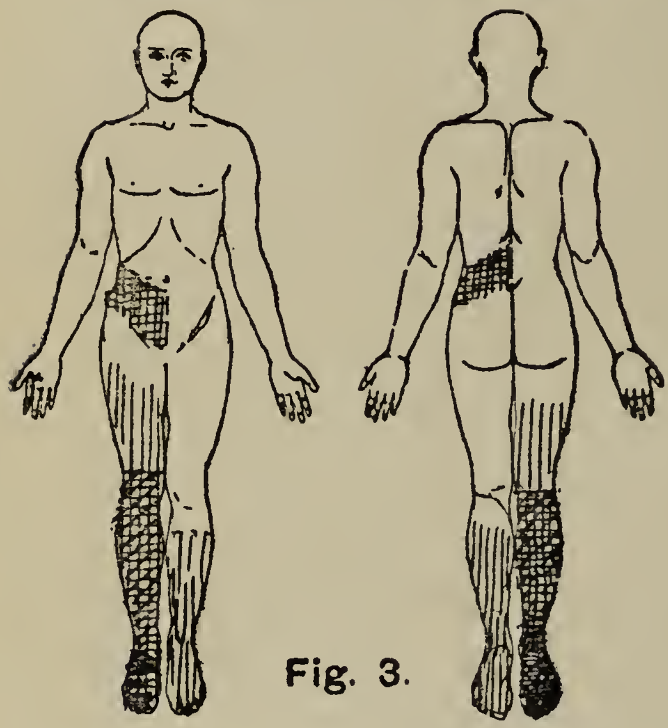

Fig. 3.

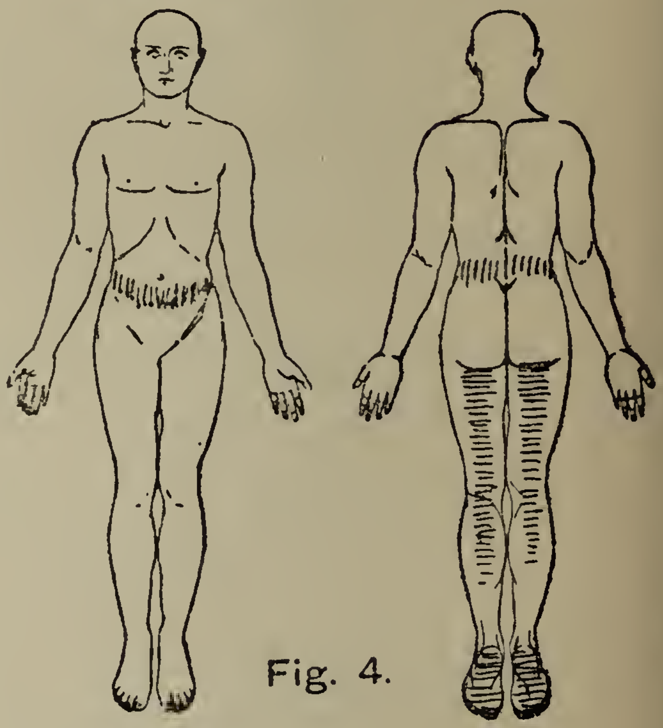

Fig. 4.

## EXPLANATION OF FIGURES.

In the figures the distribution of sensory loss to touch is indicated by vertical light shading; to pain (pin-prick) by horizontal shading; to heat and cold by oblique shading.

The depth of shading roughly indicates degree of sensory loss.

Fig. 1.—Paraplegia. Diffuse meningitis. In addition there was loss of muscular sense. Muscles of legs were wasted, with much diminished electrical reactions. Incontinence. Right knee-jerk normal, left absent. Superficial reflexes absent.

Fig. 2.—The same case after two months' treatment, when a very considerable degree of motor power had been recovered. Oblique shading indicates loss of sensation to cold only.

Fig. 3.—Paraplegia: sensory loss of moderate degree. Root-lesion at 11th to 12th dorsal. Right knee-jerk normal, left exaggerated. Right ankle-jerk normal, left ankle-clonus. Right plantar flexor, left extensor. Loss of muscular sense (partial) in left leg only.

Fig. 4.—Paraplegia. Hyperæsthesia. Zone of hyperæsthesia at level of 11th dorsal, as shaded, and on areas shaded on legs and feet. Legs spasmodically contracted and drawn up on abdomen. Knee-jerks absent. Double ankle-clonus.

in these cases the crossed analgesia does not rise to nearly so high a level upon the body as the motor palsy.

As in all these cases, thorough and especially early treatment is all-important as regards recovery, it is essential to recognise the initial symptoms. The first is generally pain, either in the back or legs, or often in the distribution of one or more nerve-roots, or a girdle-pain which, as a root-symptom, persists throughout the course of some cases. Then signs of what is now often called "intermittent claudication" may precede the paralysis, that is to say transitory attacks of paresis or even paralysis of the legs, brought on by exertion and disappearing again on resting. Transient paræsthesiæ in the legs or slight loss of control over the bladder are also important, and lastly may be mentioned again the not infrequent coincidence of signs of intra-cranial affection. In any case a lumbar puncture should be made, the spinal fluid examined for lymphocytosis and for globulin, and in case of doubt Wassermann's or Fleming's test carried out. These tests will also be valuable where the multiple and widely-spread lesions of cerebro-spinal syphilis give rise to symptoms which may occasionally simulate those of disseminated sclerosis, although if due attention be paid to the distinctive signs present of either disease there should be no difficulty in diagnosis.

Sometimes the symptoms set up by a chronic syphilitic spinal meningitis may suggest the presence of tabes dorsalis. This is of interest, because of the view held by some observers that the origin of the tabetic lesions is in a meningitis at the point of entry of the posterior roots into the cord. So far as I am able to judge this view is not borne out by the pathological data. In a chronic syphilitic meningitis, however, the Argyll-Robertson pupil is absent and there is the variability in the state of the deep reflexes already discussed. Examination of the cerebro-spinal fluid would show more pronounced lymphocytosis in tabes, and possibly a positive reaction of the fluid to Wassermann's test. Further points given by Mott are the subacute onset, more rapid development, and earlier appearance of the disease after the primary affection in syphilitic meningitis than in tabes.

There is a group of cases of spinal syphilis, clinically well defined, which was first differentiated by Erb in 1892, and is therefore often called Erb's syphilitic spinal paralysis. It is a very chronic affection, and in the cases I have seen developed late, from twelve to twenty years, after the primary infection. In some also of the cases of triplegia, in which paraplegia is slowly engrafted on to a previous hemiplegia, the disease is of this type. The onset is gradual, and the symptoms are, in brief, a spastic paraplegia or paresis combined in some with a certain amount of ataxy, often with hypotony, greatly exaggerated deep reflexes and extensor plantar reflex, sometimes pain in the back and legs or girdle-sensation, loss of sensation often absent and in all cases slight, and early involvement of the bladder. The great exaggeration of the deep reflexes with ankle and knee clonus, out of proportion to the degree of paralysis, is characteristic, as is also the combination of hypotonus with a spastic gait. The disease is slowly progressive, but sometimes remains stationary at a certain stage. Prognosis as to recovery is not good.

The pathology of these cases is somewhat unsettled. Probably the pathological lesion underlying the apparent clinical uniformity is not always the same. Erb concluded that the disease is due to a combined system affection of the lateral and posterior columns with or without a transverse lesion in the dorsal cord. A point at issue is whether a pure degeneration limited to the pyramidal tracts occurs as a consequence of syphilis and accounts for some of these cases. If so, such a degeneration on the motor side would presumably be comparable to that in tabes on the afferent side, and be classed amongst the "parasyphilitic" affections.

Harris[17] quotes Wimmer as stating that such a pure degeneration of the pyramidal tracts has only been found in four cases of those pathologically investigated, most of them presenting a combined system sclerosis. The number of autopsies recorded is, however, few. He also points out, and Williamson[18] records an actual observation in point, that since the peripheral white matter of the cord derives its vascular supply from the short arteries running in from the pia, a gummatous meningitis, by obliterating the nutrient vessels, would cause sclerosis of the periphery of the cord, and hence involve the tracts. Further, ascending and descending degenerations may start from a small patch of softening in the cord, or, as in a case of Dr. Gordon Holmes, in the pons. Nonne,[19] however, in an analysis of cases, gives, in addition to these causes, a primary degeneration of the pyramidal tracts alone, or combined with the postero-lateral tracts. It would therefore seem probable that a certain number of the cases do depend on a pure pyramidal tract degeneration. The only one of my cases of spinal syphilis which presented the Argyll-Robertson sign belonged to the group of Erb's syphilitic spinal paralysis. Wilfred Harris also states that the sign is sometimes met with in these cases. I suggest that it is in the small sub-division of this group, that depends on a pure degeneration of tracts only, and comes under the category of parasyphilitic diseases, that this sign is present.

There are rare cases of spinal syphilis in which atrophy of groups of muscles in the limbs occurs without any sign of sensory affection, and which therefore present the characters of subacute or chronic anterior poliomyelitis.

Some years ago I saw a man who had such a gradual atrophy of the small muscles of the right hand, without pain or sensory change. This recurred twice with an interval of about a year, getting well each time under mercurial and electrical treatment. Two years later he returned again with the same affection, but this time no recovery took place, and after he had attended some time as an out-patient I lost sight of him. In another case of a man aged 35, with cerebral syphilis, left hemiplegia and epileptiform fits, there was wasting of the small muscles of the left hand, and of some of those of the forearm, of gradual onset. The affected muscles gave the reaction of degeneration, but showed no fibrillary tremor. Except for some pain in the limb sensation was unaffected. A certain degree of recovery ensued under treatment. In a third case, a man aged 26, with left hemiplegia and paraplegia, wasting of the muscles of the left leg below the knee came on in the course of ten days, and was attended with considerable pain in the limb. When seen there was marked wasting of the muscles, with diminished reaction to both the faradic and constant currents. The only affection of sensation was some hyperæsthesia in the distribution of the left external popliteal nerve.

Spiller has published a case of acute anterior poliomyelitis due to thrombosis of branches of the anterior spinal artery, which showed marked thickening of their coats. He emphasises the importance of thrombosis of vessels as the cause of paralysis of acute onset in spinal syphilis. Hoffmann[20] shows that acute and chronic anterior poliomyelitis may occur in the course of syphilis, and reports a case in which a man aged 20, with signs of congenital syphilis, was so affected. Harris[21] describes three cases of syphilitic poliomyelitis, occurring very late after the primary infection, in which complete or partial Argyll-Robertson pupil was present, and in one case loss of most of the deep reflexes. In the diagnosis from progressive muscular atrophy he lays stress upon the more acute onset and presence of R. D. Examination of the cerebro-spinal fluid showed no lymphocytosis or excess of albumen.

In hereditary syphilis the cord is occasionally affected, apart from the occurrence of tabes, and such affection may either show itself in childhood, or for the first time in an adolescent who has previously been in good health. The changes in the cord in new-born infants, the subjects of congenital syphilis, have been recently described by Toyofuku,[22] and closely correspond to those found by Ranke in the brain in congenital syphilitic infants. The most striking change is a thickening and lymphocytic infiltration of the pia-arachnoid, surrounding the cord in its whole extent, and contrasting with the very slight and occasional affection of the dura mater. Equally marked is a similar infiltration of the cord itself throughout its whole transverse section. "Rod cells" were also found in addition to lymphocytes and plasma cells. Vascular disease was slight and not characteristic. The changes in the cord itself stood in no relation to those in the pia mater. The ganglion cells mostly stained normally.

Two cases of congenital syphilis under my observation, one in whom the signs of disease first appeared at 19 years of age, showed a universal swelling and infiltration of the soft membranes of the cord.

A. A., aged 21, tram conductor. Father, mother, four brothers and two sisters in good health, one brother and one sister died in infancy. Good health until aged 19. In October, 1901, he was admitted to Hospital for pains in back of head and neck of some weeks' duration, with frequent attacks of sickness, worse after food. The pain was intermittent; there was also failure of sight and weakness of legs.

On admission he complained of pains in the head, was sick and very drowsy, being roused with difficulty. Opacity of cornea, from old interstitial keratitis. Pupils dilated, acted to light and accommodation. Paresis of right external rectus. Nystagmus on looking to right. Double optic neuritis – swelling +2D. Hutchinson's teeth. Paresis left side of face. No paralysis of limbs. Right knee-jerk exaggerated, otherwise all reflexes normal. Plantar flexor. He had a fit in which left arm was convulsed.

After six weeks' treatment with mercurial inunctions and potassium iodide he went out well, except that he was a weakly youth with feeble musculature. Returned to work for some weeks, and was then laid up again, and had alternate periods of work and illness during this year, doing about four months' work altogether.

On February 8th, 1902, symptoms of weakness in the legs, headache and sickness came on again. He stayed in bed, getting worse, but managed to walk up to Hospital with great difficulty on February 12th. He was ordered to come in, but there being no bed vacant he returned home. On the 13th he lost all power in his legs, could not get out of bed, and had retention of urine; during the night the urine dribbled away. On the 14th he could not even turn in bed, and the bowels were obstinately constipated. On the 16th he was admitted, and appeared very ill, dull and heavy, cheeks hollow and sunken.

There was absolute loss of movement in lower limbs, intercostals and abdominal muscles moved in respiration. Loss of sensation below fourth dorsal segment, as shown in chart; it varied in degree. No upper zone of hyperæsthesia; arms unaffected. Bladder over-distended. No tenderness or irregularity in spines of vertebræ, no stiffness in back.

There was constant priapism. Optic discs showed remains of old optic neuritis. Cranial nerves unaffected. Knee-jerks exaggerated, Babinski's sign present on both sides. Since admission incontinence of fæces. Mental state dull and drowsy, answered questions correctly but slowly. Some pain complained of between the shoulders.

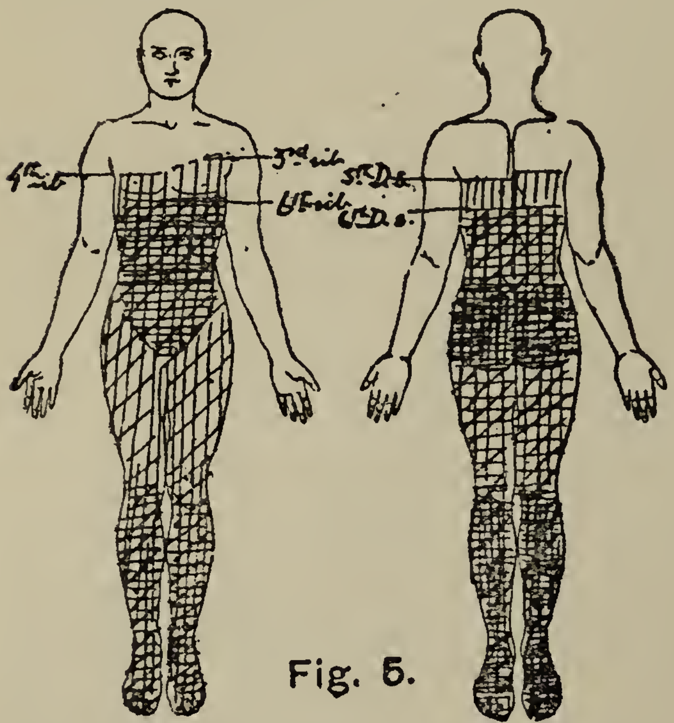

Fig. 5.—Paraplegia in hereditary syphilis. Male, aged 20. Loss of sensation indicated by shading as in other figures. In addition the vibrations of a tuning-fork were not felt over the vertebral spines below the 5th dorsal, nor over bony prominences of pelvis and lower extremities.

February 27th.—The patient has had several fits, in which he lost consciousness for a few minutes. The face and upper but not lower limbs were convulsed, the left arm being especially affected. Legs absolutely anæsthetic to light touch, but pin-prick is felt in places over them.

The fits were now preceded by a cry, and they were seen to begin in the left side of the face and left arm, and then to spread to the right arm.

During March and April he was drowsy and apathetic, the legs were absolutely powerless; the reflexes much exaggerated, with double ankle-clonus and Babinski's sign; retention of urine and incontinence of fæces continued; there was priapism; upper abdominal reflexes present, lower and cremasteric absent. The condition of sensation is given in Fig. 5. A pin-prick was felt as low as the fifth intercostal space, but localised a space too low; posteriorly, not felt below sixth dorsal spine; deep pressure and the tuning-fork vibrations were also not felt below this, and the latter not recognised on the bones of the pelvis and lower extremities.

In view of the sharp demarcation of upper limit of anæsthesia, and of the order of onset of symptoms—(1) increase of deep reflexes, (2) loss of motor power, (3) loss of sensation—it seemed probable, though I was well aware of the possibility of an extensive diffuse meningitis with secondary changes in the cord, that there might be a gummatous tumour or a localised collection of fluid pressing upon the cord in the middle or lower dorsal region, and that this might be relieved by operation. In view also of the facts that after a full trial of medical treatment the condition was getting worse, and that if unrelieved the patient was condemned to hopeless paralysis, with the prospect of death at no very distant period, it was decided to do a laminectomy. The cord was therefore exposed by the removal of the upper dorsal laminæ and spines. The dura mater appeared healthy, and on opening it a diffuse internal meningitis was found, and within this the cord itself was soft and hyperæmic. The condition was evidently too extensive to be dealt with by operation, which the patient bore well, and from which he made a good recovery. Except for the disappearance of ankle-clonus, no improvement resulted. He died about four weeks afterwards from the natural consequences of the disease.

At the *post-mortem* examination the pia-arachnoid was thickened and opaque at the base and over the cerebellum. The cerebral ventricles and iter were much distended, and full of clear fluid. The spinal dura-mater was externally normal. On slitting it up the pia-arachnoid was thickened, gummy or jelly-like—adherent to the cord and also to the dura—over the cervical and lumbar enlargements, and over the greater part of the dorsal cord. This change was most marked over the cervical enlargement, and here and over the lumbar one there was much injection of vessels, and the cord was softened.

The second case was a boy aged 10, who showed marked signs of infantilism, and in appearance looked like a little old man. He was emaciated. He could only say a few simple words when admitted, and his mental condition was so dull as not to be far removed from imbecility. He kept himself clean, and had no loss of control over the bladder. He could neither stand nor walk. The legs were drawn up on the abdomen, and the muscles were small and wasted from disuse. There was no sensory affection; the reflexes were exaggerated. He had an enormous congenital syphilitic liver, smooth, hard, and with a sharp edge. It reached the umbilicus, and the left lobe was especially enlarged to form a prominent rounded tumour in the epigastric region. So much did it resemble a tumour that an exploratory operation was done. A small piece of the liver removed at this operation showed on microscopical examination the typical histological structure of congenital syphilitic liver. Under a long course of mercurial treatment with K.I. and massage and passive movements to the lower limbs, he made a remarkable recovery as regards the paraplegia. At first he walked with a very ataxic feeble gait, but continued to improve steadily until he was able to walk and run about like a normal boy. His mental state showed a considerable degree of improvement, and he learnt to talk well, but would be still classed as feeble-minded. The liver also greatly diminished in size, and his nutrition became normal.

The discussion of syphilitic disease of the brain and cord, dealt with even as inadequately as I fear it has been done, has left me no time for the consideration of the parasyphilitic disease—tabes and general paralysis—further than to say that I agree with those who hold that they are a sequel of previous syphilitic infection.

Finally, a few words may be added as to treatment, in which the most important points are rest in bed and the prompt and efficient administration of mercury. Of course, patients in an acute or sub-acute stage, or disabled by some form of paralysis, are physically unable to get about; but complete rest is equally necessary and beneficial, although the need for it may not be so immediately obvious in cases of chronic disease during the first period of treatment. For carrying out mercurial treatment, I have used inunction, which personally I have not found difficult. Care must be taken that it is efficiently done. After about two months of daily inunctions, special care being taken of the mouth, etc., an interval is left, but it is then most important that the patient should return in about three months' time for a further course, and again at intervals of about six months for about three years. In a few of my later cases intramuscular injections of perchloride of mercury were employed. Iodide of potassium can be given in addition, especially in the later stages, in gradually-increasing doses; but though it may be administered for long periods with advantage, I do not think it is advisable to let the patient take it continuously; nor when it is necessary to push it (and it is well known that in some cases large doses are required to produce effect) have I found that any advantage is to be gained by going beyond a dose of 30 or 40 grains every four hours.

## REFERENCES.

[1] Mott, Morison Lecture, *Brit. M. J.*, 1909, i. 454.

[2] For reasons why they are not so found, *vide* Mott, *loc. cit.*

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[6] *Lancet*, 1909, i. 1512.

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[9] *Neurol. Centralbl.*, 1910, xxix., 1229.

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[13] *Brit. M. J.*, 1903, ii. 1634, and *Ibid.*, 1910, i. 296.

[14] Qnoted by Turner, Allbutt and Rolleston's *System of Medicine*, 1910, viii. 344.

[15] For a full acount *vide* Sir V. Horsley, *Brit. M. J.*, 1909, i. 513.

[16] Discussion on Syphilis, *Proc. Roy. Soc. Med.* (Neurological Section), 1910, iii. 60.

[17] Allbutt and Rolleston's *System of Medicine*, 1910, vii. 727.

[18] *Diseases of the Spinal Cord*, 1908, p. 393.

[19] Quoted by Williamson, *loc. cit.*

[20] *Jahresb. d. Neurol. u. Psychiat.*, 1910, xiii. 433.

[21] *Loc. cit.*, p. 731.

[22] *Jahresb. d. Neurol. u. Psychiat.*, 1910, xiii. 433.

# THE ARGYLL ROBERTSON SIGN IN CEREBRAL AND SPINAL SYPHILIS.

THE frequency and importance of the Argyll Robertson sign in tabes dorsalis and general paralysis is a matter of general knowledge, but there still seems some doubt as to its incidence in cerebro-spinal syphilis. In Dr. Risien Russell's[1] very interesting opening address to the discussion on ophthalmoplegia at the Annual Meeting of the British Medical Association last year he asked the pertinent questions as to how far persons who have had syphilis and have the Argyll Robertson sign have escaped tabes or general paralysis, and whether this sign is compatible with a syphilitic lesion which does not mean a tendency to progressive degeneration. It was disappointing that in the discussion which followed no decisive answers were given to these questions, desirable as it is that a point of such diagnostic importance should be settled.

Dr. Mott[2] in a discussion on syphilis in the Neurological Section of the Royal Society of Medicine said on this point: "There is one sign usually present which for all practical purposes is only met with in parasyphilis—namely, the Argyll Robertson pupil. No coarse random lesion will explain the constancy of this phenomenon; moreover, this condition, although a sign of syphilitic infection, does not occur in true syphilitic brain disease."

The Argyll Robertson phenomenon is to be regarded as an example of the selective action of a poison upon the central nervous system, inasmuch as a special group of neurones having a definite and restricted function is picked out and put out of action. It may be compared in this respect with the action of the diphtheritic poison in paralysing accommodation. The parasyphilitic affections offer other examples of similar selective action of the virus—for example, the disease of certain fibres of the posterior roots in tabes. In cerebro-spinal syphilis, however, such results are conspicuously absent, the paralyses there met with are produced as the consequence of interference with the nutrition of the neurones by occlusion of vessels from endarteritis or thrombosis, by their compression by exudation, or by destruction through gummatous tumours. *A priori*, therefore, it would be unlikely that a sign like the Argyll Robertson pupil should occur in cerebro-spinal syphilis.

In 1903, in a paper [3] on this subject based on the analysis of 37 cases of syphilis of the brain and cord, I concluded that previous syphilis is not sufficient without some further change to lead to the presence of this sign; that its presence is evidence of a degenerative process at work within the nervous system, and this process is to be regarded as a "parasyphilitic" one; but that it is reasonable to suppose that the degenerative process, of which the Argyll Robertson sign is one of the symptoms, may remain stationary at an early stage, or for a long period without further development. An example of this arrest is seen in some cases of tabes dorsalis. With some exceptions to be mentioned later, this view, if correct, would practically confine the sign to parasyphilitic infections.

In a recent analysis of 48 cases of syphilis of the brain and 21 of the cord, 69 in all, I obtained the following results with regard to the Argyll Robertson pupil. In every case there was a clear history of syphilis, or some undoubted syphilitic lesion, and, in addition, in the later cases Fleming's test was positive. Out of the 69 cases, the Argyll Robertson pupil was present in 2 of cerebral syphilis. One of these was a man of 32, apparently with syphilitic meningitis of the convexity; he had headaches, was apathetic, forgetful, depressed, with indistinct or slightly slurring speech and exaggerated knee-jerks. He showed no improvement under treatment, and his symptoms suggested the possibility of an early stage of general paralysis. The other patient was a woman, aged 45, who suffered from right facial paralysis twelve years ago, five years ago was under my care for cerebral syphilis, with right hemiplegia and Argyll Robertson pupil, and has developed on the hemiplegia a typical tabes dorsalis. In another patient there was paralysis of the right third nerve, with complete iridoplegia, the left pupil did not react to light on admission, but recovered fully under treatment. In six patients the pupil reaction to light was sluggish, but not absent, and in three of them became much more brisk under treatment. One of these suffered from epileptiform fits, both general and localised, with headache and vomiting; two from hemiplegia, with headache and vomiting; one from meningitis of the convexity, with hemiparesis, cranial nodes, and double optic neuritis; the fifth was a patient with hereditary syphilis, with cerebral symptoms and optic neuritis; and the sixth was a patient suffering from syphilitic cerebro-spinal meningitis, with hemiplegia and intense optic neuritis. So that optic neuritis, in varying intensity, was present in three of the six cases with a sluggish reaction; optic neuritis does not, of course, abolish the light reaction. Of the 21 spinal cases, in one the light reaction was sluggish, and in two the Argyll Robertson sign was present. Of the latter, one was a rather remarkable case. The patient was a man, aged 32, who had had left hemiplegia two years before, from which recovery was not complete. When admitted, he was dull, apathetic, and had some mild delusions as to place and as to his circumstances. The cord affection corresponded to Erb's syphilitic spinal paralysis, and was of very gradual onset, with the usual affection of the bladder, great exaggeration of deep reflexes, and double extensor plantar reflex. The pupils were very small. He made, under mercurial treatment, an unexpectedly good recovery, both as to his mental and physical state, and was able to return to work. The Argyll Robertson sign persisted. In the other case the cord affection was of the same kind, with no affection of sensation, no ataxy, and no symptoms except slight incontinence beyond those clinically referable to degeneration of the pyramidal tracts ; the disease was also of very gradual onset.

It is an interesting point that the only cases presenting the Argyll Robertson sign amongst my cases of syphilitic disease of the cord are cases belonging to the clinical group of syphilitic spastic paraplegia, first described by Erb. Wilfred Harris[4] states that in Erb's syphilitic spinal paralysis " sluggishness of pupils, or even complete reflex iridoplegia may, however, be met with." Although presenting the same clinical features, it is probable that these cases do not all own the same pathology. If some of them are due to a primary degeneration of the pyramidal tracts as a result of syphilis, then they would represent a degeneration of the efferent neurones analogous to that of the afferent fibres in tabes, and come under the parasyphilitic affections. Harris quotes Wimmer as stating that in only 4 cases examined pathologically was there a pure degeneration of the pyramidal tracts, but it may be added that the records of autopsies are few. From the recorded cases Nonne[5] gives the following four conditions as underlying this form of paraplegia : (1) Chronic myelitis in patches, with ascending and descending degenerations ; (2) these changes combined with a primary degeneration of the pyramidal tracts ; (3) degeneration of the pyramidal tracts only ; and (4) a combined primary postero-lateral tract degeneration.

I suggest that it is with the group of pure degeneration of the pyramidal tracts that the Argyll Robertson sign will be found associated, and that the condition is a parasyphilitic one.

In connexion with syphilitic spinal disease, it may be added that Dr. W. Harris[6] found "complete or partial Argyll Robertson pupil" in three cases of chronic syphilitic poliomyelitis. These cases were a very late sequel of syphilis, in one of the three appearing twenty-five years after infection.

In analysing the above cases, I have not taken into account a unilateral loss of the light reaction, because it is then more difficult to exclude local causes; in four or five of the cases unilateral loss occurred in association with paralysis (complete or incomplete) of the third nerve on the same side. Moreover, if the Argyll Robertson sign is rightly considered as the selective action of a poison, both pupils should be affected. So far as my cases go, therefore, they entirely support the contention that this sign is not a symptom found in pure cerebro-spinal syphilis, and that its presence is an index of a degenerative process at work in the nervous system.

The contrast with tabes and general paralysis, in which the sign is present in about 70 per cent. or over of the cases, is too striking to call for further remark.

In testing the cases no further precaution was taken than always to place the patient opposite a good light (daylight), cover both eyes, and see that they did not accommodate.

I have referred throughout to the fully developed Argyll Robertson sign only, because merely sluggish pupils, although in certain connexions suggestive, have not the same clinical significance. Further, it is now certain that in recent cases and under efficient mercurial treatment an absent light reflex may sometimes be regained.

There are one or two other conditions under which the Argyll Robertson sign may be present, but the associated symptoms should prevent any error in diagnosis. Thus, Dr. Farquhar Buzzard,[7] in the discussion on ophthalmoplegia, mentioned cases in which the sign was present in cysts of the third ventricle, and in tumours of the optic thalamus extending to the corpora quadrigemina. Other observers have also noted it in lesions of the corpora quadrigemina, but it does not invariably accompany them. It is also present in optic atrophy, but not in optic neuritis.

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[4] Allbutt and Rolleston's *System of Medicine*, 1910, vol. ii., p. 728.

[5] Quoted by Williamson, *Diseases of the Spinal Cord*, London, 1900, p. 344.

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[7] *British Medical Journal*, 1910, vol. ii., p. 1319.

# ON TOXIC POLYNEURITIS OF THE MOTOR TYPE.

In the following cases of multiple neuritis objective disturbances of sensation were absent, and though there was a certain amount of pain, in one case considerable pain, the symptoms were essentially those of motor paralysis. Instances of this type of neuritis, excluding, of course, those of single nerves, are not at all common. The great majority of cases of multiple neuritis are those of alcoholic neuritis, in which sensory disturbances form one of the most striking clinical features. In the early stages of the motor type of polyneuritis, when the disease is spreading and invading successive groups of muscles, the difficulty of diagnosis from an ascending paralysis of spinal cord origin, and also from certain cases of anterior poliomyelitis may be difficult. Moreover, many of the most characteristic features of multiple neuritis, as seen in the common form due to alcohol, are absent or inconspicuous. Thus in alcoholic neuritis women are far more often affected than men, and women especially between forty and fifty years of age.. The legs are involved first, and in the majority of cases the arms escape or are comparatively slightly affected, whilst pains, tenderness of nerves and muscles, and peripheral loss of cutaneous sensibility are prominent, and these symptoms, together with certain other features, especially the mental changes, which form the well-known Korsakoff's syndrome, and the cardiac weakness, due to the action of alcohol on the heart-muscle, all contribute to make up a characteristic and striking clinical picture. Again, in acute toxic polyneuritis the cause is generally obscure, and often there is no clue to its exact nature.

Except in those cases which follow influenza, or some such infective disease, the onset is insidious, may take place during apparently good health, and the absence of constitutional disturbance seems to negative the idea of a microbic infection as the cause.

During the first few days of a case of toxic polyneuritis of the motor type the resemblance to ascending or Landry's paralysis is close, so that one may have to postpone decision as to the exact nature of the illness, and may have considerable anxiety as to the event, owing to the gravity of the prognosis in the latter disease.

In the majority of cases, however, of polyneuritis the onset and progress of the paralysis is slower than in a typical case of Landry's paralysis, and in the course of the second or third week, if not at the onset, the paralysis begins to be definitely greater at the periphery of the limbs, if not in all four extremities at first, yet either in the arms or in the legs, and to predominate in the extensors, whilst alterations in the normal electrical reactions of the most affected muscles begin to be evident. These changes in electrical reactions precede the wasting which, indeed, in some cases is not very marked throughout the illness.

The diagnosis from acute anterior poliomyelitis is not so difficult, as in the great majority the sufferers from this disease are much younger than those from acute toxic polyneuritis, and if in exceptional cases the age cannot be taken into account in distinguishing between the two affections, there are the decided signs of constitutional disturbance at the onset of acute poliomyelitis, the characteristic pains on passive movements of the joints, the absence of such symmetrical paralysis, the escape of a muscle or group of muscles in the otherwise paralysed limb, the recovery of some muscles soon after the onset, and the frequent presence of a large lymphocytosis in the cerebrospinal fluid.

The first case I report is one of the senile type of the disease, and corresponds to the usual descriptions of this form in its insidious course, and absence of pain or other sensory disturbance; but although sensory symptoms are usually comparatively inconspicuous, they are rarely so completely absent as in this instance, in which also there was not the marked arterio-sclerosis which is generally associated with senile neuritis. The diagnosis presented no difficulty, as the signs of polyneuritis were characteristic by the time the patient came under observation.

This patient was an emaciated man aged 72. The family history was good. He had never had any illness of any kind, had always been strong, healthy and temperate, and worked very hard as a blacksmith.

Six weeks previous to admission he felt quite well on getting up, but on going to work noticed that his right leg dragged; he was, however, able to stay at work without inconvenience during the whole of that day, but on going to bed he had to be helped upstairs, as both legs were so weak that he had great difficulty in getting upstairs even with help. He had a good night, but on waking the next morning he found the weakness had so increased in the legs that he could not stand, and had spread to both arms, so that he could not raise himself in bed. There was no constitutional disturbance of any kind, and no pain. The limbs felt "dead" and numb. Since this time he has remained *in statu quo*, confined to bed and practically helpless. Sphincters, speech, swallowing and special senses unaffected.

On admission he was very helpless and unable to move himself in bed. Tongue clean. Pulse 104. Respiration 24. Temperature subnormal. The few teeth remaining were bad. No blue line on gums. There was a moderate degree of atheroma of the vessels. Both legs were powerless except for slight movements at left hip. The feet were dropped, and toes flexed. There was also double wrist-drop, the fingers were slightly flexed and could not be extended. With great effort the right arm could be moved feebly at the shoulder, and very weak movements of the left were possible at shoulder and elbow, with feeble flexion of wrist. He could not feed himself nor use the hands for any purpose. The head and neck could be moved freely. The muscles of all limbs were wasted, especially the extensors of wrist, fingers, ankles and toes.

Diaphragm and intercostal muscles acted well.

Electrical reactions. Loss of reaction to Faradic current in extensors of left wrist and fingers, interossei of right hand, anterior tibials and peronei muscles of both legs; very feeble reaction to strong current in long extensors of right wrist and fingers and muscles of thumbs. The flexor muscles responded but feebly in arms; calf muscles also reacted feebly. All muscles reacted to the constant current, but the extensors gave a slow wave, and ACC=KCC. In the flexors the response was normal.

There was no affection of sensation to pain, light touch, heat or cold. Sense of position and of movement of limbs unaffected. No muscular tenderness.

There was a slight tremor of the left arm when movement was attempted. No cramps or spasms.

*Reflexes.*—Deep reflexes absent. Superficial:—abdominal and cremasteric present, plantar absent.

The paralysis was entirely flaccid in type.

Cranial nerves unaffected. Pupils equal, acted well to light and accommodation. Optic discs normal. Thoracic and abdominal organs normal. Urine normal. Sphincters unaffected.

He remained in the hospital one week, his condition being unchanged, and then refused to stay any longer.

In the next case the diagnosis was for some little time doubtful, owing to the completeness of the paraplegia, and to the extensors not being predominantly affected until late after the onset. For a time also the electrical reactions were unaltered. Wasting of the muscles did not occur for a long time, and was never conspicuous throughout the illness. In fact, the slightness of the wasting in muscles which remained paralysed for months was remarkable. The pains in the cervical spine soon after the onset also introduced a doubtful element in diagnosis. The time taken for recovery, a little over twelve months, shows what is to be expected as to duration in a severe case of this type, and also that even if little progress is made for six months this need not preclude complete recovery. The case, indeed, illustrates the fact that recovery may be perfect, if due care is taken throughout the illness in the prevention of contractures and of unfavourable position of the limbs; so favourable a result is hardly seen in any other form of paralysis. Throughout the illness there was no affection of sensation, beyond at one time a doubtful and partial anæsthesia to light touch on the outer sides of the feet. Efforts were made to find out the nature and source of the toxin, but without success. Examination of the blood and cerebro-spinal fluid and bacteriological examinations of the fauces and urine gave no clue to it.

John B., aged 34, a joiner, had always enjoyed good health, except for a mild attack of jaundice when in the Argentine five years previously. He was in a very healthy district, and never had malaria. He had never had syphilis, and had always been very temperate. Eight weeks previously he had a sebaceous cyst removed, which left a discharging sore for three weeks and then healed well. He had no sore throat. On September 14th, 1913, he had cramp in the muscles of the right leg, followed next day by stiffness in both legs, then by weakness. The stiffness and weakness gradually increased until the 18th, when his feet tingled and became so numb that he could not tell their position, and consequently found great difficulty in walking. On the 19th he could not walk to his work, but managed to get there on his cycle. On the 20th he found he was unable to walk without support, as he lost his balance, and was unable to tell the position of his legs unless he looked at them. On this day numbness and tingling, with weakness, also appeared in both hands. On the 23rd he felt a feeling like a " lump of lead " in the abdomen. From this date the weakness of the limbs steadily increased, and he was confined to bed until his admission to hospital on October 2nd.

On admission he was well nourished and healthy-looking. The pulse was 88, the respiration, tongue and temperature normal. The bowels moved by aperients. The thoracic, abdominal organs, and urine were quite healthy. He was unable to stand, but could just move the legs slightly at knee and hip-joints, otherwise they were paralysed. The paralysis was flaccid. There was no foot drop. The muscles were not wasted : they all reacted to a Faradic current. The constant current gave so much pain that it could not be used. There was no affection of sensation to pin, cotton wool, heat or cold. The sense of movement and of position was not lost.

*Reflexes.*—The deep reflexes in the legs were absent, in the arms absent or very feeble.

*Superficial Reflexes.*—Plantar absent, cremasteric present, abdominal very feeble. No pain on passive movement of limbs. Slight loss of power in forearm and hands. Special senses and cranial nerves unaffected. No optic neuritis ; no alteration in speech or swallowing. Sphincters unaffected. Spinal column normal : no tenderness over spines. Cerebro-spinal fluid on lumbar puncture gave a slight excess of cells, lymphocytes and endothelial cells. Wassermann's test negative for blood and cerebro-spinal fluid. A swab from throat showed no Klebs-Löeffler or diphtheroid bacilli. Blood normal : no leucocytosis. Bacteriological examination of urine negative. Stools appeared healthy. At this stage it was impossible to make the diagnosis as to the exact nature of the lesion causing the slowly spreading paralysis of the legs. The mental condition was quite clear and good.

During the next two weeks he suffered much pain in the neck and back of the head. At the end of this time paralysis of both lower extremities had become almost complete, except for very slight movement at the hip-joints ; there was now marked foot-drop on both sides. Numbness (without objective loss of sensation) and loss of power in the hands had increased, each grasp registering only 15 on inner dynamometer scale, and the deep reflexes in the arms were now completely abolished. There was still no muscular wasting, and his condition was otherwise unchanged. A few days later the abdominal reflexes disappeared, and he complained much of a girdle pain. Three weeks after admission electrical reactions showed in the legs diminished reaction to interrupted current, especially in dorsiflexors of feet and long extensors of toes. To constant current the calf muscles gave normal reaction. The quadriceps extensors only reacted to a very strong current. Right, KCC = 10 ma. Left, KCC = 14 ma. ACC = 18 ma. Peronei and tibiales antici on both sides, KCC = 1 ma. ACC = 2.5–3 ma., and the contraction wave was slow.

On November 6th there were slight signs of wasting in the leg muscles, especially marked in the anterior muscles of the legs below the knee. The muscles were now also distinctly tender to pressure, and there was pain on passive movements of the ankles. There was a definite reaction of degeneration (R.D.) in peronei and tibiales antici muscles, and also some loss of sensation of movement and of position in left leg. Sensation otherwise unaffected.

By the end of November the paralysis had increased in the forearms and hands, which had become very weak, and the muscles of the forearms and the interossei appeared to be wasting. He could feed himself, but not cut up his food. There was indefinite and slight loss of tactile sensation on outer borders of feet. The only movement left in the lower extremities was internal rotation at hip-joints. The muscles of the lower extremities gave a slow, very feeble response to a very strong Faradic current; those of the forearm, especially extensors, and of the hand also reacted badly, whilst the arm muscles gave a normal response. The nerves responded well. The leg muscles (below knee) now all showed reaction of degeneration to constant current. He remained much the same until the middle of January, when the forearms and hand began very slowly to gain power. The small muscles of the hands had wasted, and showed occasionally fibrillary twitchings. During this time all the muscles had become tender to pressure. The foot-drop had increased, and the legs were now placed in splints. Sensation remained normal, and the bladder unaffected. There was continued constipation. He could not sit up in bed. The diaphragm was never involved. All the reflexes in the limbs were lost, but the cremasteric and abdominal reflexes, though feeble, were present. The only muscles of the legs that responded now to the Faradic current were the right gastrocnemius and tibialis anticus, and adductors of left thigh.

During March he began slowly to improve, regaining first power in arms and hands, and then in hips. The muscles were no longer tender. In April he could sit up in a chair, swing his legs backwards and forwards, and slightly extend the left leg. There was, however, yet no recovery of power in muscles below the knee. In May he could very nearly stand without support, could walk with the aid of a walking machine, and by the end of the month could walk by pushing a chair in front of him. The foot-drop still remained for a long time afterwards. The subsequent course of the case has been one of very slow but steady recovery, so that he is now able to get about, and is going to take up some light employment. The knee-jerks are still absent.

In the following case, as in the preceding instance, the cause of the disease could not be ascertained, the onset was insidious, whilst the patient was apparently in perfect health. His occupation exposed him to extremes of heat and cold, and often involved heavy muscular work.

The distribution in this case is peculiar, and differs from the two just reported. The disease began in the upper extremities, with weakness two days later in legs, not proceeding to actual paralysis for three to four days longer. Moreover, in the legs the thigh muscles were those chiefly affected, and those below the knee at first escaped, to be involved later. The paralysis in all four extremities was, however, strictly symmetrical, and from the onset was in the arms of the peripheral type, extensor paralysis predominating, and the extensor muscles alone showed commencing reaction of degeneration (R.D.). In the lower extremities the quadriceps extensors are especially affected, and show more wasting and alteration of electrical reactions than any other muscles of the body. In spite of the somewhat unusual distribution of the muscular paralysis, there is no doubt of the case being one of toxic polyneuritis. As in the other cases, there is a complete absence of sensory affection, subjective or objective, apart from pains in right shoulder at the onset. This was the only fatal case.

Alfred T., aged 50, a marine fireman. He had never had any illness of any kind, and denied any venereal disease. He had six healthy children. He had been moderate as to alcohol, but smoked about one ounce of tobacco daily.

Three weeks before admission, whilst in perfectly good health, he had pains in right shoulder; on the following day he went to work, but felt weakness in both arms and hands; on the third day the weakness had so much increased in the arms that he was unable to work. By this time he felt some weakness of the lower extremities, which did not increase, and he was able to get up and sit about until three days later, when, on getting out of bed in the morning, his legs gave way and he fell to the ground. He remained in bed practically helpless for ten days longer, and was then admitted to hospital. There were no symptoms of constitutional disturbance, no pain after the first day; some tingling and feelings of pins and needles in forearms, hands, legs and feet. He had had some headache, the mind has been quite clear. Profuse sweats occurred at night, but no fever. Sphincters unaffected.

He did not come into contact with lead in his work.

On admission he was a well-built, healthy-looking, well-nourished man. No blue line on gums. Gums and teeth healthy. He lay in bed on his back, with arms across the abdomen. Except for some movements in the shoulder, chiefly due to pectoralis, serratus magnus and trapezius muscles, the upper extremities were completely paralysed. When they were raised there was double wrist-drop. He could not sit up, turn, or move himself in bed. In the lower extremities slight rotation of hips and slight dragging up of legs by thigh muscles were possible, the ham-strings and extensors of legs were paralysed, but he could flex and extend ankles and toes freely but feebly; with this exception the lower extremities showed complete paralysis, could not be raised off the bed, and were useless.

The paralysis was of the flaccid type. Slight wasting of muscles was noted in the left quadriceps extensor, perhaps also in the right, in the extensors of wrists and fingers, and in the muscles of the thumbs and the abductor indicis. It was nowhere conspicuous, and the other muscles preserved their normal size.

There was no paralysis of any of the cranial nerves. Pupils equal, dilated, reacted to light and accommodation. Optic discs normal.

Speech and swallowing normal. Movements of head and neck unaffected.

The chest moved well in respiration, the movements of the diaphragm were perhaps a little feeble.

Sensation to touch, pin-prick, heat and cold everywhere normal. He retained the sense of position of his limbs; passive movements were not painful, and the muscles nowhere tender.

*Reflexes.*—Deep; biceps and triceps jerks present on both sides, wrist, knee and ankle jerks absent.

*Superficial.*—Abdominal absent, cremasteric present, both plantar present and flexor in type.

Bladder unaffected; bowels constipated. Pulse 80, regular. Respiration 24.

Thoracic and abdominal organs normal. Urine 1026, no albumin, no sugar, loaded with urates.

Cerebro-spinal fluid under normal pressure and clear. Cells normal, a few lymphocytes only being present. Wassermann's test negative.

*Examination of Blood.*—Red cells 6,000,000 per c.m., hæmoglobin 90 per cent., leucocytes 19,000 per c.m., polymorphs 69 per cent., mononuclears 50 per cent., eosinophils 1 per cent.

One week after admission electrical reactions were as follows:—

*Interrupted current.*—Normal response in all muscles except the extensors of wrists and fingers and quadriceps extensor on each side, where a strong current was necessary, and to a less degree in small muscles of hands.

*Constant current.*—Right arm, in long flexors and extensors, KCC = ACC, 7 and 5 ma. respectively. Left arm, long extensors, wrist and fingers, KCC = 8 ma., ACC = 6 ma. Flexors, wrists and fingers, KCC = 5 ma., ACC = 8 ma. Right abductor indicis, KCC = 3 ma., ACC = 7 ma. Left KCC = 6 ma., ACC = 7 ma. Legs, right quadriceps extensor, KCC = 12 ma., ACC = 10 ma. Left quadriceps extensor, KCC = 18 ma., ACC = 12 ma.

Other muscles gave normal reactions. The patient was very tolerant of both currents.

Ten days after admission the condition of the arms as regards paralysis was unchanged, wasting of the forearm muscles was more evident ; the diaphragm was slightly affected ; there appeared to be little if any power in the abdominal muscles, to which the constipation was partly attributable ; the thigh muscles were slightly more wasted ; and the paralysis had slowly spread to the legs, so that hardly any movement of feet and toes was possible, and the right foot was dropped. Plantar reflexes present, but very feeble. Other reflexes absent. In other respects his condition was unaltered. Sensation good everywhere.

During the next few days the action of the diaphragm became increasingly feeble, the respiration was quickened, the pulse became increasingly rapid and weak, the heart's action feeble, and he had difficulty in swallowing. The movements of the tongue and speech were unaffected, the facial and oculomotor nerves were not involved. He died of heart failure two weeks after admission. A *post-mortem* examination was not permitted.

The fourth case is that of a woman aged 33. She had been married about eighteen months, and before marriage was completely worn out by nursing her mother through a long illness. Her father died of diabetes. She had had no previous illness, and had always been temperate. The illness began with pains and loss of power in the legs two to three months before her confinement, which took place about three months before admission to hospital. For two months previous to confinement she lay in bed with her legs drawn up, and screamed if they were extended. Delivery was normal, no instruments being used. After it the paralysis spread to the arms. The pains in the legs began some time before she lost power in them. There had been no pains in the arms, but they felt dead or numb. The limbs rapidly wasted, and for two months before admission she had been helpless and unable to feed herself. From the fifth month of pregnancy and continuously since she had suffered from salivation.

On admission she was emaciated, there being no subcutaneous fat, and the muscles everywhere showed an extreme degree of wasting. She lay on her left side with her knees fully flexed, and thighs flexed on abdomen. The legs were contracted in that position, and she screamed when they were moved.

Appetite good. Tongue furred and tremulous. Pulse 120, respiration 20. Temperature normal. Bowels constipated.

The teeth were very bad, many carious stumps, gums spongy, with pus around roots of teeth. No blue line on gums, no evidence of any source of lead poisoning.

The salivary glands were not enlarged: there was an almost constant flow of saliva. The thoracic and abdominal organs appeared to be normal. Urine normal. The pupils were unequal, but reacted well to light and accommodation. Optic discs normal. There was paresis of muscles of left side of face. Otherwise the cranial nerves were normal, and swallowing and speech unaffected.

She complained of some pain in the neck, but movements of head and neck were free.

*Arms.*—She could raise the arms, and flex, and extend the elbows partially. All the muscles of arms and forearms were much wasted. There was double wrist-drop, the small muscles of the hands were wasted, the thumbs and index fingers were in position of extension, the other fingers flexed. The left index finger could be flexed, and the thumbs could be partially opposed and adducted: otherwise paralysis was complete.

*Trunk.*—The abdominal muscles and those of the back were much wasted; she could not sit up.

*Legs.*—Glutei were wasted, and there was great wasting of all the muscles of the legs, especially below the knee, where the anterior tibial and peronei had practically gone, leaving a hollow. The ham-strings and calf muscles were relatively well preserved. There was complete double foot-drop and all the toes were in position of flexion.

The only movements possible were feeble flexion of the hips, and slight movement of the legs. From contraction of tendons and adhesions in the joints neither hips nor knees could be passively moved beyond a right angle; and such movements caused much pain.

None of the muscles were tender, and there was no tenderness over the course of the nerves.

*Electrical Reactions.*—To Faradism muscles of arms acted well; those of forearm, especially extensors, feebly. Small muscles of hands reacted well; the quadriceps extensor and ham-string muscles gave a weak reaction. The calf muscles contracted to a strong current. No reaction was obtained from the peroneal nerves, peronei, tibialis anticus and long extensors of toes. The constant current gave her great pain, and the reactions could not be well taken, but no reaction of degeneration was found save in the muscles of the anterior and outer aspect of legs.

The deep reflexes were absent, abdominal present, plantar absent. There was nowhere any affection of sensation to light touch, deep pressure, pin-prick, heat or cold. The sense of localisation of touch and of position of limbs was not lost. The sphincters were unaffected.

The patient's mental condition was childish, she cried very easily; but there was no loss of memory or confusion of ideas.

The first point in treatment was to get the limbs into better positions. She was therefore anæsthetised, numerous firm adhesions in and about the hip, knee, and ankle joints were broken down, and the legs placed on straight splints. The upper extremities were also freely moved at all joints.

Subsequent treatment was by gentle massage and passive movements and Faradism, with maintenance of the limbs in suitable postures in order to prevent dragging on the paralysed muscles. The salivation gradually ceased.

After five months' treatment in hospital she had recovered sufficiently to return home.

This is an example of the somewhat rare though well-recognised form of multiple neuritis which occurs in pregnancy, or during the puerperium. If the onset is during pregnancy, the symptoms may become more marked after labour, which, as in this case, may take place normally. The disease appears especially in patients who suffer severely from the vomiting of pregnancy. In puerperal cases the cause is generally held to be a septic infection; in those arising during pregnancy it is attributed to an intoxication related to the physiological processes of that condition, or, by others, *e.g.* (Huber) to infection from a previous puerperium or from uterine disease (Oppenheim). In some cases the progress of paralysis is rapid, and the disease may take the form of Landry's paralysis. The possibility of alcohol as an additional factor in causation must be remembered. In this case there was no evidence of alcohol, but the patient was exhausted by long nursing before she became pregnant.

The prognosis in this form of neuritis is as a rule favourable.

The last case is one in which the chief symptom was inco-ordination, combined, as the disease went on, with a certain amount of definite paralysis, the latter being symmetrical and of the peripheral type. The presence of actual muscular weakness is important in the diagnosis from tabes dorsalis, because it is not a feature of this disease until, at any rate, a late stage is reached. The ataxy in this case reached an extreme degree, as marked as I have ever seen it in a bad case of tabes dorsalis, and was, indeed, so severe as to render the limbs useless. Moreover, it was attended by marked hypotonus, so that the joints and limbs could be placed in very abnormal positions without causing discomfort. The loss of the muscular sense and of that of position of limbs was also pronounced. Some doubt has been thrown on the existence of severe ataxia in multiple neuritis, it being held that errors in diagnosis have been made, and that the cases are really examples of tabes dorsalis, in which the association of disease of peripheral nerves with that of the posterior columns of the cord in tabes dorsalis, which is of frequent occurrence, is more than usually pronounced and extensive.

Dr. Judson Bury sums up his study of the question[1] by saying (1) that ataxia is rare in peripheral neuritis even when cutaneous and muscular sensibility are profoundly affected; (2) that it occurs occasionally when signs of muscular weakness and of diminished cutaneous sensibility are slight or absent.

Undoubtedly marked ataxia is a rare feature of multiple neuritis, and especially when, as in this case, there is no affection of common sensation. This is the only instance of the kind and degree that has come under my observation. In the diagnosis in this case I would lay stress on the complete absence of all signs of affection of the spinal cord, and on the presence of a definite amount of paralysis in the legs of the peripheral type, symmetrical, and accompanied by some muscular wasting, and on the recovery that took place in a comparatively short time. These are the essential points in the diagnosis of ataxia due to polyneuritis. One may also remark on the affection of the facial nerve, and its recovery after a short time. This is the cranial nerve which is most commonly affected in multiple neuritis.

Another feature was the presence in the wasted muscles of fibrillary tremors or twitchings, also an unusual symptom. This symptom was also present in the second case. It is to be expected that it should sometimes occur in these severe cases of multiple neuritis in which the whole of the lower motor neurone, including the anterior horn cell, is more or less affected. The cause in this case may either have been alcohol, in spite of his statement that he had been temperate for some years, or an infection through the urinary tract, as he had B. coli pyuria, or possibly the action of the latter upon nerves previously sensitised by excessive indulgence in alcohol.

John P., æt. 49, was admitted to the hospital in July, 1916, complaining of loss of power in the legs and arms. The onset was gradual, and began in the left leg a few months before: during the last month the arms and hands had become affected.

He was a traveller, and had had no previous illness except a chill (? influenza) twelve months before. For twenty years, up to the age of 42, he had been accustomed to drink about a bottle of whisky daily in the course of his business; since that age, according to his own statement, he had been a teetotaller. For some months he had been unable to get about, and had been confined to bed for over one month. He had never had syphilis.

He was a well-nourished man, with florid complexion and dilated venules on cheeks, and watery eyes, the vessels were thickened and tortuous; the pulse full and of high tension; the heart's apex beat was one inch outside the nipple line, the aortic second sound accentuated; the urine (sp. gr. 1010) showed no sugar or albumin; the lungs and abdominal organs appeared healthy.

There was no blue line on the gums; the tongue was tremulous but not wasted: its movements were inco-ordinated. He could not stand or sit up in bed, could not use his hands to feed himself, or hold a newspaper. When he tried to pick up anything the movements of the hand and arm had a peculiar swooping character. All movements of the hands, arms, legs and feet were wildly ataxic in character, and this was greatly increased when his eyes were closed. Without sight he had no idea of the position of his limbs. There was no absolute paralysis, but the extreme ataxy practically meant that he could not make use of his limbs for any purpose. Though no movements of the lower extremities were entirely absent, yet there was considerable loss of power in them, in addition to the ataxy, and this loss of power was chiefly in the muscles moving the ankle and foot (periphery of limb). This was not the case in the upper extremities, where the right grip measured 30 and the left 20 on inner scale of dynamometer. The muscles of the arms, hands, and trunk were not wasted. On the other hand, the glutei and all muscles of lower extremities, except the ham-strings, were wasted, and the wasting was especially marked in the anterior muscles of the thigh, and tibialis anticus and peronei group. The big toes were dropped, but not the feet.

There were irregular muscular twitchings almost amounting to fibrillary tremor in the most wasted muscles. The muscles all reacted to both interrupted and constant currents, but in the wasted muscles the response to the former was diminished, and to the latter increased, without any reversal of the normal formula. The muscles were flaccid, with loss of tone: in the legs there was considerable hypotony, it being possible to put the joints into very abnormal positions without causing pain. The muscles were not tender, but there was slight tenderness over nerve trunks.

*Reflexes.*—Superficial: abdominal and cremasteric present, plantar doubtful. The deep reflexes were absent in both arms and legs.

Sensation to light touch (cotton wool), pain (pin-prick), heat and cold was everywhere unaffected. Localisation of sensation was also good. The sphincters were unaffected throughout. Pupils equal, reacted to light, accommodation and consensually. Optic discs normal. Other cranial nerves normal. Special senses normal.

During September he had two rigors and fever, with the appearance of a quantity of pus in the urine due to a B. coli infection of urinary tract. The symptoms cleared up under treatment in the course of a month, but B. coli with a few pus cells persisted in the urine. After the first rigor there appeared partial paralysis of the right facial nerve, which gradually disappeared during the next fortnight.

The general treatment was by massage, electric baths, and systematic training in movements of the limbs. For a time the wasting of the leg muscles continued, and to such a degree that the calf muscles had the feeling described by Gowers of " a bag of worms." Fibrillary twitching in the muscles most wasted was often noticed. At the end of September he began slowly to improve, the arm muscles first recovered their tone, the movements became less inco-ordinate, and he was able to use the arms and hands. Improvement in the legs followed more slowly, the fibrillary twitchings ceased, movements improved, and the wasted muscles very gradually recovered. By December he was able to stand and walk with support, and in January, 1917, with the aid of sticks. Though not recovered, for recovery of the wasted muscles would take a still longer time, he was so much improved and so much more able to help himself, that he left the hospital in this month. The deep reflexes were still entirely absent. There were no mental changes throughout the illness. There were no shooting pains, no joint or skin lesions, and no tendency to bed sores.

## REFERENCE.

[1] Allbutt and Rolleston's *System of Medicine*, 1910, vii. 449.

# NERVOUS AFFECTIONS OF THE SIXTH AND SEVENTH DECADES OF LIFE.

## Part I.—Diseases of the Spinal Cord.

Mr. President and Fellows, — My first and most pleasant duty is to offer my best thanks to Sir Thomas Barlow and to express my deep sense of the honour that he has conferred upon me by asking me to give this lecture, and also to associate with him in my acknowledgments the present distinguished occupant of this chair for his approval of the subject which I have taken.

In selecting the sixth and seventh decades of life it may be thought that a somewhat arbitrary division of age has been made. On consideration, however, it will be seen that this period has certain marked characteristics of its own. One might have taken as the lower limit the age of 45, which Dante fixed as the end of the period of youth, but that would involve in most women the inclusion of the climacteric, which I thought better to avoid. It may be held, although there are many notable exceptions to the contrary, that the period of the greatest activity of the originative and creative faculties is over by 50, yet the ensuing years are those in which experience is ripe and judgment most sound, and in which use has made the performance of difficult tasks easy and certain. Though it is true that the most original work is not done between 50 and 70, yet a very large share of the skilled work of the world, that which requires the full development of the mental powers, is carried on by persons of this age. It is, therefore, not unimportant to consider what diseases tend to cut short or to destroy the usefulness of these years, and, conversely, from what diseases they are exempt. The beginning of this period is that of full maturity, and the end brings us to the advent of old age.

Many nervous diseases run a very long course, and we should therefore expect to find that the nervous affections of this period will be made up of some which began at an earlier age and of others, fewer in number, whose incidence is entirely contained within it. It will be convenient to consider them separately, noting their incidence and also any peculiar features or modifications in their course which may occur at this time of life. I do not propose to include mental affections.

## SPINAL CORD.

The diseases of the spinal cord between 50 and 70 years of age are both numerous and important. Tumours of the cord present no special features at this age; secondary metastases in the cord itself to cancer elsewhere are very rare. I have seen two examples of secondary growths in the cauda equina; the primary growths were in the breast and prostate respectively.

### *Myelitis.*

Myelitis is not a common disease after 50. In 156 cases reported as myelitis, acute or subacute, excluding pressure-myelitis, 18 per cent. occurred after this age. The age given in hospital reports probably represents very nearly that of onset, as chronic cases with secondary degenerations would come under other designations—*e.g.*, spastic paraplegia. This relative infrequency after 50 might be expected from the common causes of myelitis, which are chiefly some acute infection or intoxication in which the myelitis may be either primary or secondary, and syphilis. No doubt syphilis is the cause of a larger number of cases than is generally recognised. Taylor and Buzzard[1] state that syphilis is responsible for the great majority, probably 80 per cent., of cases of myelitis. The term myelomalacia is more accurate than myelitis for many cases. After 50 the infective disorders are rare, and if the view stated below is correct that spinal syphilis is also uncommon after this age, the relative infrequency of myelitis after this age is accounted for. One might, perhaps, anticipate an influx of cases of myelitis, or rather myelomalacia, in later life, due to vascular occlusion from arterial degeneration, but large patches of softening in the cord seem rarely to result from this cause ; the contrast in this respect with the frequency of areas of softening in the brain is remarkable. Arterio-sclerosis in the cord seems to affect the smaller vessels and to produce small sclerotic foci or diffuse areas of degeneration.

### *Lesions of the Posterior or Lateral Columns.*

The diseases of the spinal cord which are especially characteristic of this age are diffuse lesions of the posterior or lateral columns, mostly degenerative. These are the cases formerly grouped together as the " combined scleroses." In some symptoms due to disease of the lateral columns predominate, and the clinical picture is then that of spastic paraplegia. This is a very definite clinical syndrome, but due to various pathological states. In other cases the posterior columns are chiefly affected, and many are of pathological rather than of clinical interest, as the changes in the cord either give rise to no symptoms, or else these are overshadowed by the more urgent ones due to the general disease in the course of which they occur. Such are the degenerations of the posterior columns found in cachectic states, in carcinoma, in glycosuria or diabetes, the slighter forms of the cord degenerations of pernicious anæmia, and also those found in some cases of chronic cystitis and enlarged prostate. In all the lower part of the cord is solely or chiefly affected and the predominant symptom is paraplegia, or paraplegic weakness with ataxy, with or without some generally not profound, sensory affection.

### *Paraplegia.*

Cases of paraplegia of this kind are found recorded under the names of spastic, ataxic, or senile paraplegia, combined sclerosis, or subacute combined degeneration. Unfortunately these terms are not always used in the same sense, whilst cases of one group shade by degrees into those of another, and except in the case of subacute combined degeneration convey no very clear idea of the pathological changes. For instance, under such a name as ataxic paraplegia will be found included quite distinct diseases, whilst spastic paraplegia merely indicates the predominant clinical feature irrespective of its pathological cause. An important step forward in differentiation was the separation of subacute combined degeneration, both clinically and pathologically, from amongst these various conditions by the work of Russell, Batten, and Collier.[2]

With the proviso that the above designations as given in reports of cases are not mutually exclusive and only afford a rough idea of the age incidence, I find that of 114 cases of spastic and ataxic paraplegia, combined sclerosis, and subacute combined degeneration, 38 per cent. occurred between 50 and 70 years of age. If spastic paraplegia is excluded for the reason that it will comprise many old-standing cases of lateral sclerosis secondary to myelitis and other causes, the proportion between these ages is higher, 49 per cent., and reaches its highest point in subacute combined degeneration.

Dr. Collier[3] in his excellent account of this disease states as to the age of onset that the extremes are between 30 and 65 years, and that the highest incidence is reached between 55 and 60. Of 11 cases under my observation, in most of which the diagnosis was confirmed *post-mortem*, the age in 9 was between 53 and 64. There was no definite cause for the disease in any; in two cases it appeared after severe diarrhœa and vomiting, and one patient had had syphilis. As to the association with anæmia, 3 of the patients suffered from pernicious anæmia, 3 from anæmia distinctly of the secondary type, and 4 were not anæmic.

None of these varieties of combined sclerosis of the cord can be regarded as true system degenerations, understanding by this term the degeneration of fibres anatomically and physiologically connected, in which disease is not due to local changes in the cord, but to some profound change in the body generally with a specific action on certain spinal tracts. The true system degenerations appear earlier in life and are often hereditary or familial. They are represented after the age of 50 by cases of degeneration of the lateral columns which exceptionally occurs in tabes dorsalis, of amyotrophic lateral sclerosis, and by an occasional survivor of Friedreich's disease, and of hereditary spastic paraplegia.

Hæmatomyelia of spontaneous and non-traumatic origin is rare at any age. Of von Pfungen's[4] 10 cases, 4 were between 60 and 65. As this is the age of cerebral hæmorrhage it might be expected that the cord would also be liable to hæmorrhages, but this is not the case, the reason probably being that the circulation in the cord does not suffer from rapid and great alterations in pressure.

I may briefly refer to weakness in the legs or paraparesis as occasionally a symptom of chronic uræmia in elderly persons. This may be the first sign of kidney disease for which the patient seeks relief. In three cases which I saw the symptoms, of gradual onset, consisted of weakness in the legs with a feeble, tottering, or uncertain gait. There was no affection of sensation, the deep reflexes were exaggerated, the superficial normal; there were constipation and difficulty of micturition. The affection lasted from three to six months before severe general symptoms of uræmia appeared.

Senile paraplegia is a name used for paraplegic weakness due to diverse pathological changes. For the most part the sufferers are beyond the age we are considering. A variety has, however, been described by Oppenheim,[5] which he attributes to arterio-sclerosis of the cord and to perivascular sclerotic changes especially in the white matter, and forms one variety of the group of "combined scleroses." According to Purves Stewart,[6] the cases so affected can hardly be called senile. The ages of Hirsch's cases varied from 44 to 65. The symptoms are those of a slowly progressing spastic paraparesis, ultimately leading to contraction of the limbs, with increase of deep reflexes. Less usual are sensory disorders and sphincter paralysis (Oppenheim).

Sir William Gowers also described under the name of simple senile paraplegia a condition occurring especially in persons over 50 characterised by simple weakness of the legs with slowness of movements, but without wasting, sensory disorder, or alteration of reflexes, and resembling paralysis agitans without tremor.

Spastic paraparesis or even paraplegia may in later life be due to cerebral affections; for instance, small patches of softening on each side of the pons or bilateral disease of the cortical leg centres, causing degeneration of the pyramidal tracts.

### *Pressure Paraplegia.*

Among the causes of paraplegia from compression of the cord, caries of the spine, hypertrophic cervical pachymeningitis, and internal pachymeningitis involving a great extent of the cord, and probably of syphilitic origin,[7] are seldom met with after 50. According to Bruns, extramedullary, benign, solitary and slow-growing tumours are most frequent between 40 and 60 years. These are the tumours most favourable for operation. In 4 cases over 50 in my care 3 were in the cervical and 1 in the lumbar region; the latter and one of the former were removed, with recovery of power. The most important cause of a compression paraplegia in later life is cancer of the vertebræ; the cases are almost all over 50, and the growth nearly always secondary. The primary tumour is most frequently in the breast, but may be in the prostate, stomach, uterus, or other organ. On account of the agonising pain which often attends it, this is one of the most terrible of diseases. Occasionally a case is seen in which little pain is suffered, but this is exceptional. The typical feature of the pain is that it is brought out or increased by movement, is in abeyance during rest, and is localised. Sometimes early, but more often later, in the course of the disease pains from pressure on posterior nerve roots may occur; these are not so much affected by movement, are lancinating, and pass down the course of the nerve.

The diagnosis in the early stage is often difficult. The symptoms may be vague, and one is not justified in making such a grave diagnosis except on certain grounds. An X-ray examination may clear up the diagnosis in a doubtful case, but not always. Late in the disease, when the patient is cachectic, wasted, has deformity of the spine or the characteristic shortening of the trunk due to involvement of several vertebræ, and pressure paraplegia, the diagnosis is obvious. Cases may not be diagnosed before paraplegia occurs, and the onset of paraplegia may be almost sudden from the development of a patch of softening in the cord at the site of compression. In one case of a small scirrhous tumour of the breast the primary tumour was not noticed before paraplegia occurred. The discovery of the primary tumour or history of its removal is the most valuable aid to early diagnosis of cancer of the spine. A history of a considerable interval between the removal of the growth and the paraplegia is important. Many years may pass between operation for the primary growth and the development of metastases in bone.

The absence of some of the more characteristic symptoms of malignant disease leads to a failure of early diagnosis; thus there may be no wasting, and patients may even become fat from enforced inactivity; tenderness or pain on percussion over the spines may be absent even when the patient complains of intense pain on movement; and deformity of the spinal column may not occur until late in the illness. The early pains may be set down to rheumatism or hysteria. The latter mistake is especially apt to be made when the disease occurs in a woman known to be formerly hysterical, or when the attacks of pain are intermittent. In some cases both the pains and the difficulty of carrying out certain movements may entirely disappear for a time, and Oppenheim lays especial stress on the errors of diagnosis likely to arise when pronounced temporary improvement occurs.

A rare cause of pressure paraplegia in later life is a limited osteo-arthritis of the vertebræ. Various forms of osteo-arthritis of the spine are well known, and I refer only to those cases in which a paraplegia, generally painful, is caused by an osteo-arthritic lesion limited to a few vertebræ. Such a case is described by Bailey and Casamajor,[8] in which the existence of an extramedullary tumour seemed probable as the cause of the paraplegia, but at the operation the laminæ and spinous processes of the twelfth dorsal were found thickened, abnormally soft, and greyish in colour, and were removed. Pathological investigation showed chronic osteo-chondritis with new bone formation. The patient completely recovered. The authors emphasise the value of an X-ray examination in such cases.

In a man of 65 whom I saw there was paraplegia of sub-acute onset apparently due to a transverse myelitis at the level of the eleventh dorsal roots. At operation the eighth, ninth, and tenth dorsal laminæ had undergone some form of sclerosing osteitis with great thickening, that of the ninth being fully one inch thick.

### *Tabes Dorsalis.*

Tabes dorsalis, the most common disease of the spinal cord, fairly maintains its frequency in the sixth decade of life. Of 700 cases the proportion living over 50 was 24 per cent. Byrom Bramwell's[9] statistics give the age of onset in 263 cases; 9.7 per cent. occurred in patients over 50 and 1.9 per cent. in those over 60 years. Cases in which the onset occurs after 45 as a rule run a more favourable course. The longer the interval after infection before symptoms of tabes occur the less acute the course of the disease. It is well known that where optic atrophy is an early sign the disease is often mild and non-progressive. It is not necessary to give instances of the long duration of the milder forms of this disease. In some cases of tabes the symptoms are slight and do not advance; in another group the disease is more pronounced, but the average duration before the patient is incapacitated is fifteen years (Malaise).

Tabes shows a decided falling off after 50 as compared with 30–50, and a very marked fall after 60. The cases over 50 comprise: (1) stationary and latent cases; (2) others only slowly progressive—of these the onset in 30 per cent. took place between 40 and 50 years of age; (3) cases which begin after 50. In some of these there was a late syphilitic infection after 40 years of age, but in others the interval after infection was twenty to thirty years or even longer.

Arthropathies seem to be present in a larger proportion of cases than in younger patients; in several cases the character of the work as involving the especial use of certain joints seemed to determine the site of the arthropathy. Aortic disease is more frequent in elderly tabetics, and other complications are hemiplegia or recurrent paralysis, either monoplegic or hemiplegic, due to syphilitic disease of the cerebral arteries. In some of these patients the signs of tabes may be first discovered when the patient seeks advice for one of these complications. Cases following an acute course with severe ataxy are rarely met with after 50. The prognosis as to life is not bad, except in aortic or vascular disease or cystitis following old-standing difficulties of micturition. Cystitis is sometimes due to a B. coli infection of the urinary tract. In its onset and recurrent phases this infection in old cases of tabes may be very severe and directly threaten life.

### *The Muscular Atrophies.*

The myopathic forms of muscular atrophy do not affect the period of life under consideration, but from the long course run by some cases, sometimes as long as thirty or forty years, there will be a few survivals. Of 100 cases of various forms of muscular dystrophy 3 or 3.5 per cent. were over 50 years of age. On the other hand, the myelopathic forms, progressive muscular atrophy, bulbar paralysis, and amyotrophic lateral sclerosis, are relatively frequent after 50. Although the essential pathological process in these diseases is probably identical, there are sufficient differences clinically between progressive muscular atrophy and amyotrophic lateral sclerosis to justify the retention of the names, although it must be admitted that cases in which the disease is absolutely confined to the lower motor neurons are seldom seen.

The clinical difference between the three forms also appears in the age incidence. The order of frequency of these diseases after 50 is ; (1) bulbar paralysis, in which the large majority of cases occurs after this age ; (2) progressive muscular atrophy ; and (3) amyotrophic lateral sclerosis. In 60 cases of progressive muscular atrophy 30 per cent.

occurred between 50 and 70, and of 63 cases of amyotrophic lateral sclerosis 12 per cent. were found between these ages.

With regard to the etiology in myelopathic muscular atrophy, there is good evidence that syphilis may be the cause in some cases. Head and Fearnsides[10] consider that muscular atrophy of syphilitic origin can be divided into two groups—(1) examples of meningo-vascular syphilis, and (2) cases analogous to tabes dorsalis and primary optic atrophy. For the most part the cases in both these groups will fall before the age of 50, though it would be expected that those in the second should be the later of the two. In several cases of progressive muscular atrophy in elderly patients I noticed that the atrophy started in muscles or groups of muscles which were chiefly used in the patient's occupation, and may presumably have become exhausted. The rate of progress of the atrophy was more rapid in these cases. The disease steadily spread beyond the muscles first affected, so that there was no question of a mistake in diagnosis for a limited atrophy of muscles due to occupation. Is it possible that a muscular atrophy from occupation starting from over-fatigue of special muscles tends in an elderly person to spread widely, whilst in those younger it remains limited to the muscles involved in the particular action concerned? The occurrence of these forms of atrophy after 50 is not obviously connected with arterial disease, for this was not more pronounced in these patients than in normal persons of the same age.

Some rare cases of progressive muscular atrophy run a subacute course, and are especially met with in the elderly. Oppenheim[11] classes them apart as subacute and chronic anterior poliomyelitis. He suggests a toxic cause, and says that care must be taken in diagnosis to exclude toxic polyneuritis. Other writers assign the cause to traumatism, and Oppenheim quotes the observations of Schmaus-Sacki, who showed that injuries by causing disturbances of the lymphatic circulation may lead to local lymph stasis and tissue necrosis.

Of two well-marked cases of this affection, both in men in good circumstances and of previous good health, one was aged 67. Three weeks after a heavy fall weakness of the left hand and arm began and steadily increased; two months later he had very little use of the upper extremity, and its muscles generally showed atrophy with fibrillary tremor. Five months after the accident the atrophy had greatly increased, both upper extremities and the neck being now involved. The disease shortly afterwards spread to the bulb, and he died quite suddenly. The other patient was aged 66. He had been overworked for some time before the onset of the disease. The distribution of the atrophy, as in the other case, was practically confined to the upper extremities. The course of illness was four months, and he also died suddenly. Lastly, may be mentioned the very occasional occurrence of atrophy of the small muscles of the hand in connexion with a cervical rib even so late as 50 years of age.

### *Disseminated Sclerosis.*

Disseminated sclerosis is essentially not a disease of the period of life under consideration. It generally begins much earlier, but as it may run a long course, there will be a certain number of survivors after 50. Moreover, it is well known to be peculiarly liable to remissions, sometimes of very many years' duration, and the final outbreak may exceptionally be deferred to quite late in life. An extreme example of this occurrence is given by Purves Stewart.[12] The remissions may be of such duration as almost to amount to recovery from the disease; possibly such remissions may occasionally even be permanent.[13] Allowing for a source of error from the fact that in common diseases only exceptional cases are recorded, instances of the onset of this disease in patients over 50 are very uncommon. In 536 cases from various sources irrespective of age of onset the number over 50 years was from 4 to 5 per cent. The few cases in which the onset occurs late in life seem often to present exceptional features, and are therefore of importance from the point of view of diagnosis.

The rare form in which disseminated sclerosis runs its course with muscular atrophy and may resemble amyotrophic lateral sclerosis is considered by Schnitzler[14] to affect older patients and to run a more rapid course. He gives a case, aged 53, in which the clinical diagnosis was amyotrophic lateral sclerosis, but the necropsy showed a typical disseminated sclerosis.

There are also cases such as those reported by Bornstein[15] in two women aged 60 and 62 respectively. The clinical signs were those of a subacute transverse myelitis, and pathological examination showed areas of multiple sclerosis together with marked changes in the vessels. Their exact relation to the more regular types of disseminated sclerosis has still to be determined.

### *Syringomyelia.*

In syringomyelia the large majority of cases occur between 20 and 45 years of age. The disease, however, is met with at all ages, and considering that it is one of the rarer nervous diseases, fairly often over 50. Out of 135 cases 23 per cent. were between 50 and 70. Hospital statistics give a rather lower percentage (about 17 per cent.) than reports of special cases. On the view now generally held that syringomyelia is due to a gliosis of the cord, it is interesting to compare the age incidence with that of glioma elsewhere. Dr. H. H. Tooth[16] in 127 cases of glioma of the brain gives 11 per cent. with onset between 50 and 70. Syringomyelia may run a very long course; thus Oppenheim mentions a patient alive at 68 in whom it began at 18. Other instances are on record where the duration was 48, 40, and 36 years. Such cases form a certain proportion of those over 50. On the other hand, the onset may be after that age; this happened in 13 out of 69 cases. Sometimes the disease suddenly takes on an acute phase, or progresses afresh in later life after quiescence for long periods. Syringomyelia may almost certainly be latent and suddenly start into activity. Although there is still a difference of opinion on the point, the evidence that the cause of this activity is often an injury is strong.[17]

Fries,[18] in an inquiry into syringomyelia in old persons, concludes that it does not differ from that at earlier ages. Pathologically it is characterised (1) by the replacing of gliosis tissue by connective tissue (*Bindegewebe*), which originates from the adventitia of diseased vessels, and (2) by the formation of cavities in the lateral columns of the cord not connected with the central canal and due to patches of softening. He attributes the progress of the disease in old persons not only to gliosis, but also to the formation of cavities through arterio-sclerosis. The first appearance of syringomyelia in later life or the sudden aggravation of symptoms may be due, at any rate in part, to secondary vascular changes in the cord and to hæmorrhages.[19] Hæmorrhage from diseased vessels into cavities formed as above described may easily occur, and has been actually found as the cause of a sudden aggravation of the disease in elderly people.

Other cases occur in which the symptoms are clinically those of syringomyelia, but own an entirely different pathology, being due to the formation of cavities in the cord as a direct result of hæmorrhage from vessels with degenerated walls. When syringomyelia originates or starts into fresh activity late in life it is generally progressive.

It may be added that the origin of destructive disease of the joints in an atypical syringomyelia is probably more frequent than is generally recognised. A remarkable case came under my notice. A woman aged 62 five and a half years previously had her left leg amputated above the knee because it was so extremely contracted that it caused great pain and the heel was forcibly pressed against the anus and hindered defæcation. Subsequently the right leg became contracted and flexed across the abdomen. When I saw her this leg had been straightened by an osteotomy on the femur and tibia. At the operation the bones were found to be remarkably brittle and atrophic. She had also slight atrophy of the small muscles of the hands, and areas of loss of sensation to pain and temperature, with retention of tactile sensibility, were found on the face, the chest, forearms, and hands.

### *Neuritis.*

Of the various forms of multiple neuritis that due to alcoholic excess is, of course, by far the most common, and is also the one that has the most striking age incidence. In 250 cases of multiple neuritis taken from various sources only 10 per cent. occurred over the age of 50. 75 per cent. of these cases were between the ages of 30 and 50.

In 45 cases under my care 24, of whom 18 were women, were between the ages of 40 and 53 years. There seems to be a special incidence of alcoholic neuritis during the climacteric. The cause of this may be found in the nervous disturbances from which women suffer at this time. The mental depression and the feelings of nervous exhaustion or lassitude, which are such common features of the climacteric, would tend to induce the less strong-minded to seek relief in alcohol. The nervous changes of the climacteric may possibly impair the nutrition of the lower neurons, and render them more susceptible to the poisonous action of alcohol. As to symptoms, I think that the characteristic mental symptoms of Korsakov's syndrome are more frequent and pronounced in this group than in cases at an earlier age, and also that there is—very constantly—affection of the heart muscle.

Of the less common forms of multiple neuritis the glycosuric is perhaps relatively the most frequent after 50. The etiology is often a mixed one, and may consist of gout, glycosuria, and alcohol. In several cases of glycosuric neuritis in persons between 50 and 60 the patients were heavy drinkers, and in them alcohol, if not the chief, was a large contributory cause. In any case of supposed glycosuric neuritis a possible alcoholic origin should be excluded.

A rare but grave form is acute or subacute toxic polyneuritis. Instances of this disease may occur at any age, though the majority fall between 20 and 45. Of 13 cases under my care, four occurred at the ages of 72, 68, 50, and 49 respectively.[20] A widespread paralysis of acute or subacute onset due to toxic polyneuritis may follow an ascending course, and constitutes one group of the cases classed under Landry's paralysis. In the majority the presence of decided sensory changes, "glove" and "stocking" anæsthesia, pains, and muscular tenderness are distinctive of polyneuritis, but there is one form which affects the lower motor neurons almost exclusively, and leaves the sensory almost or entirely unaffected. The early diagnosis from the spinal form of ascending paralysis may then be difficult.

It remains to mention the cachectic forms of neuritis, and especially that which develops in connection with carcinoma, for the majority of such cases will naturally fall between the ages of 50 and 70. The symptoms as a rule are of slight intensity. Towards the end of this period the senile form of multiple neuritis, which in some instances is referable to arterio-sclerosis or atheroma, appears. In this variety, according to Oppenheim, neither paralysis nor sensory symptoms are very marked; others, however, have described cases in which pains and hyperæsthesia were prominent features.

Brachial neuritis is in my experience relatively not infrequent between 50 and 65, and this also applies to anterior crural neuritis, which often seems to be started by slight traumatisms or by muscular effort.

Of 50 cases of sciatic neuritis, many very severe and of long standing, and all of them sufficiently bad to compel the patients to seek treatment in hospital or to confine them to bed, 27 cases occurred between 30 and 50, and 23 cases between 50 and 70 years of age, 16 of the latter falling between 50 and 60. Rheumatism and gout, with exposure to cold and wet, and excessive muscular exertion are the chief causes. In my experience the prognosis is not distinctly worse nor treatment less successful in patients over 50. The treatment adopted in nearly all the cases was immobilisation by means of the long splint.

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## PART II.—DISEASES OF THE BRAIN.

Passing now to diseases of the brain, I do not propose to deal with meningitis except briefly with the tuberculous variety, and that on account of the peculiarity of its symptoms in adult cases. Meningitis due to pus-producing organisms becomes uncommon after 50; when it occurs as a primary infection the diagnosis is now greatly facilitated by lumbar puncture. Perhaps the most frequent form is the pneumococcic, which may either be primary, or a complication of pneumonia, or one feature of a general pneumococcic infection. I shall omit chronic internal pachymeningitis, as it is rare apart from mental disease.

### *Tuberculous Meningitis.*

Tuberculous meningitis in persons over 50 is very exceptional. Of 560 cases of tuberculous meningitis four had passed this age. There were also eight cases between 40 and 50. In adults it occurs chiefly as the termination of chronic pulmonary tuberculosis. In Seity's statistics, quoted by Sir Thomas Barlow,[1] in which childhood is excluded, of 126 cases between the ages of 16 and 60 years, 4 occurred after 50 years and 15 between 40 and 50. Dr. W. B. Warrington[2] states that there is generally an incubation period of three to four weeks, and then rapid onset of coma ending in death within a week. The early symptoms may be deceptive and mistaken for early mental disease, hysteria, or delirium tremens. He quotes Jaquet,[3] who found that of 204 fatal cases of chronic phthisis, 7 died from tuberculous meningitis between 41 and 68. In several the symptoms developed with great suddenness, and two patients were picked up unconscious in the street. Jaquet gives the average duration as ten days. In a man aged 52 under my care the last illness began with obstinate vomiting lasting seven days, then there was a remission for two days, when diplopia and intense headache came on, followed by coma, fatal on the fourteenth day. There was no retraction of the head and no optic neuritis. Well-marked signs of pulmonary tuberculosis were present.

Two other cases were aged 47 and 46; both died in coma after a last illness of seven and ten days respectively. The primary disease was in one a tuberculous orchitis.

### *Cerebral Hæmorrhage and Thrombosis.*

The most common of all nervous affections between 50 and 70 years of age are those due to disease of the cerebral vessels, which are not, strictly speaking, nervous diseases, but the secondary effects on the nervous tissues of disease of their arteries. The causes and methods of prevention, therefore, belong to diseases of the vascular rather than of the nervous system. The subject of vascular disease of the brain is too extensive to be considered here. With regard to the age incidence, of 500 cases of cerebral hæmorrhage the onset was between the ages of 50 and 70 in 321, or 64 per cent., and of 110 cases of cerebral thrombosis in 67, or 60.9 per cent.

### *Cerebral Tumours.*

With regard to the age incidence of intracranial tumours, there are available the very valuable statistics compiled by Dr. Tooth.[4] The age of onset of the first symptoms, verified or not by operation or *post-mortem*, in his 500 cases was between the ages of 50–70 in 7.2 per cent. In 238 of these the nature of the growth was verified by operation or *post-mortem*; of these the age of onset was between 50 and 70 in 9.6 per cent. The gliomata constituted 49.2 per cent. of the total, and of these 10.27 per cent. occurred at from 50–60 and 0.7 per cent. at 60–70 years of age. The carcinomata were few in number, but the percentage between 50 and 70 was nearly 40. In a further number of 485 cases which I have collected from various sources, similarly verified or not, the proportion between 50 and 70 is rather higher, 13 per cent.

Bruns mentions the infrequency of cerebral tumours in the later years of life, and states that he has only seen one case over 60.

Of 18 cases of intracranial tumour in persons over 50, in 12 of which the diagnosis was verified by *post-mortem* or operation, in one the tumour was cerebellar, in two it was in the cerebello-pontine angle, and in the remainder in various parts of the cerebrum. Three of the patients were over 60 years of age. In several of the cases the sudden onset of symptoms suggested some intracranial circulatory disturbance. Thus in four cases the first symptom was an attack of vertigo resulting in a fall and occurred during active exercise.

As to special symptoms, optic neuritis was well marked, attacks of vertigo especially frequent, and apart from the situation of the growth mental changes were prominent. In two cases the intracranial growth was secondary to cancer of the breast. The period of life under consideration is, of course, that in which cancer is most frequent. Affection of the nervous system by cancer is generally through secondary metastatic growths. The order of frequency of metastases is (1) vertebræ, (2) bones of skull, (3) brain, and (4), very rarely, spinal cord. These secondary growths may occur in any part of the brain and are often multiple. They may form diffuse or localised tumours. Symptoms may be pronounced and dominate the case, or, on the other hand, absent or overshadowed by those due to growths in other organs, and the intracranial metastases only discovered *post-mortem*.

The diagnosis of a cerebral tumour in a person over 50 is often difficult. In the case of a primary tumour the symptoms may be attributed to other diseases of the brain more frequent at this period of life. Thus for the mental disturbance produced by a growth other causes may easily be assigned; headache and vertigo are common complaints in persons over 50, and of various origin; and hemiplegia or monoplegia would rather suggest vascular disease, though the gradual onset of hemiplegia is always suggestive of a tumour.

To sum up, an intracranial tumour is relatively uncommon in persons over 50, and still more so in those over 60; when it occurs diagnosis may be more difficult than in younger persons.

## CEREBRO-SPINAL SYPHILIS.

Turning to syphilis, the proportion of cases of cerebral syphilis over 50 is relatively small. Of 261 cases 9 per cent. were over 50 and only 3 cases over 60 years of age; these include 60 personal cases in which the number over 50 was 8. The maximal frequency of the disease falls between 30 and 45, or according to Neumann,[5] whose data, however, are taken from *post-mortem* results, between 30 and 39 years. The interval between infection and the onset of nervous symptoms is in the majority within 10 years, often, of course, much earlier. The statement that has been made that the older the patient the shorter the interval between infection and the appearance of cerebral symptoms seems not to be correct.[6]

In cases over 50 a certain number are due to late syphilitic infection; in three of my cases the age of infection was 35, 44, and 46 respectively, and signs of cerebral syphilis appeared from 12 to 15 years later. In the remainder the late onset of cerebral disease is due to a long interval after infection. The symptoms do not seem to differ greatly from those in younger patients. In two of my cases in which the interval between onset and infection was very long affection of the cranial nerves was the chief feature. Head and

Fearnsides[7] give a case aged 56, syphilis at 44, and another aged 47, in which a third nerve paralysis was the chief affection, and a third aged 55, syphilis at 25, in which many cranial nerves and also some spinal roots were affected. Vertigo, as in cerebral tumours in later life, is often a prominent symptom. The question as to the part played by previous syphilitic infection in the production of disease of the cerebral vessels—*i.e.*, as to the proportion of cases of apoplexy or hemiplegia occurring after 50 which are due to vascular disease as the direct result of a previous syphilitic infection—is a very important one, but I am not able to give exact statistics.

It is now generally recognised that fits indistinguishable from those of idiopathic epilepsy may occur as a result of cerebral syphilis. So far as I have been able to ascertain, the age of onset as a rule is before 50. I have seen two cases over 50: one, a man aged 60, syphilis at 46, had attacks resembling petit mal; and the other was first affected by repeated severe epileptic seizures at 54.

Syphilitic affections of the spinal cord are relatively still more uncommon after 50 than those of the brain. It is stated by Head[8] that "there is no period after infection when the patient may not be attacked by a paraplegia." Generally the symptoms of spinal syphilis follow somewhat early after infection. This is especially the case in syphilitic meningo-myelitis, which may occur within six months of infection. Oppenheim[9] states that in the great majority spinal syphilis develops within six years. The relation of syphilis to myelitis has been already discussed.

It might be thought that Erb's syphilitic spastic paraplegia would be found late in life. These cases are certainly of mixed origin. The exact nature of the lesion can only be determined by a *post-mortem* examination. Pathological investigation seems to show that only a small number described as syphilitic spastic paraplegia depend on a pure degeneration of the pyramidal tracts. Dercum[10] has recorded a case clinically corresponding to this disease, in which the pathological change was a meningo-myelitis, in a man aged 66. My cases have been between 35 and 50. As, however, this variety runs a longer course than other syphilitic affections of the spinal cord, there would be a greater probability of survival after 50.

In 3 out of 35 cases of various forms of spinal syphilis the patients were over 50. One was a man aged 53 who contracted syphilis at 22, with onset of spinal symptoms at 40. Affection of spinal roots gave rise to the chief symptoms. The disease was probably a chronic meningitis, and was remarkable for its long duration. The second case was clinically a transverse myelitis in the lower dorsal region of the cord. The onset was subacute at the age of 56, and syphilitic infection occurred at 37. The third was of spastic paraplegia in a woman aged 62, whose husband had tabes.

To sum up, the onset of cerebral syphilis after 50 is not common, of spinal syphilis rare, and for both still more rare after 60.

## THE NEUROSES.

I now pass on to consider some of the neuroses. Of *migraine* the commonly received opinion is that the sufferers from it either lose their attacks or that these become mitigated in later life, and that in women this relief is to be expected after the climacteric. A confident prognosis is often given to this effect. Speaking generally, this opinion seems to be correct and migraine is uncommon, at any rate in a severe form, after 50. Such a prognosis can, however, only be given on general grounds ; it is impossible to say in an individual case that lapse of years will give relief. Many patients suffer from more frequent attacks during the climacteric, and in a certain number an increase in the frequency and severity of the attacks dates from this epoch. Heredity to the disorder itself, and to other neuroses, is marked in most cases of migraine and is generally pronounced in those cases that persist in later life. Overpressure of work, especially mental work, is also a cause of its persistence.

Does migraine lead to permanent paralysis later in life or to persistence of one of the symptoms of the paroxysm as a permanent defect? Where especially a premonitory hemiopia has been a constant feature of the paroxysm is permanent hemiopia likely to result? I have seen one instance of this in a woman aged 35, and another in a man aged 54, but he had also arterio-sclerosis, high blood pressure, and glycosuria. J. J. Thomas[11] gives three examples of hemiopia becoming permanent. There are also instances on record of permanent paralysis following migraine, but these are mostly in persons under 50. Most of the patients showed disease of the vessels, but others were young, with presumably healthy arteries. Such consequences of migraine seem to be so rare as to be of little practical importance, and do not especially occur after 50. In the uncommon form of migraine in which the attack is followed by a transitory paralysis of one limb, or even by a hemiplegia, there may be more reason to fear permanent paralysis. Elsewhere[12] I have recorded the case of a family of which many members suffered from this form of migraine through three generations, and since writing the account one of the patients has, at the age of 51, become permanently hemiplegic.

Headache in connection with a contracted granular kidney may closely simulate migraine. Thus, a patient with well-marked signs of contracted kidney of some years' duration first began to suffer at the age of 55 from attacks of headache exactly resembling migraine, with ocular prodromata in the left eye, in which there was commencing albuminuric retinitis. As migraine never occurs *de novo* late in life, no mistake in diagnosis should be possible, for though in some patients there may be an intermission for years careful enquiry will elicit a history of former attacks. On the other hand, I have come across several instances in which lifelong sufferers from migraine developed a granular kidney after 50, the headaches becoming more severe but retaining their original form.

An important question is whether migraine leads to epilepsy in later life. It is a matter of common observation that migraine and epilepsy not infrequently occur in different members of the same family, either in collaterals or in previous generations. The similarity of some features of the two diseases is also remarkable. The further assumption of anything like identity between them is, however, not justified. Occasionally a patient is subject to both affections.[13] Oppenheim states definitely that it has never been proved that one of these conditions may develop into the other. Personally, I have not met with migraine developing into epilepsy in later life.

### *Epilepsy.*

It is well known that the frequency of epilepsy diminishes as life goes on, but it is also true that epilepsy may begin at any age. I cannot give extensive statistics, but of 100 consecutive out-patient cases 6 per cent. had their first fit after 50, and in 100 consecutive private patients 9 per cent. Especial care is necessary in the diagnosis of idiopathic epilepsy in later life to be sure that the case is not one of an epileptiform attack, symptomatic of some underlying disease. This especially applies to Jacksonian epilepsy, for after 50 localised epileptiform attacks from the partial closure of a diseased cerebral artery are not uncommon. As to direct heredity in cases of epilepsy of late onset, Gowers gives 26 per cent. in those which begin after 40, and Turner 10 per cent. in cases arising between 41 and 70.

Finckh, however, puts the proportion as high as 66 per cent. In eight personal cases in which the onset was between 52 and 65 years there was a hereditary history in two only.

In late epilepsy men were more frequently affected than women. Idiopathic epilepsy between the ages of 50 and 70 comprises: (1) Cases in which the disease persists throughout life; (2) cases in which the patient suffered from fits in childhood or early life, and then was free for a number of years, with a subsequent reappearance late in life; and (3) those in which the onset is after 50.

The first occurrence of epileptiform fits after 50 years of age may be connected with the presence of arterio-sclerosis and a high blood pressure. These cases cannot therefore be brought into the category of idiopathic epilepsy. Whether the fits are due directly to the high blood pressure or to the toxæmia which produces it is a moot point, but as cases of hypertension are common after 50, and epileptic attacks rare, there is probably some other adjuvant factor in the causation. The attacks may be severe general epileptiform ones or those of minor epilepsy (petit mal). Some of these cases are undoubtedly due to a contracted granular kidney, but in others, the kidney is not involved, and they cannot be regarded as uræmic.

In late epilepsy, supervening at an age when the wear and tear of life has often produced changes in the blood-vessels, it would be anticipated that the strain on the cerebral circulation produced by a fit should sometimes lead to hæmorrhage. Of this I have seen two instances: one was in a life-long epileptic who at the age of 70 died of hæmorrhage from a cerebral artery which ruptured in the course of a fit. In the other case the first fit took place at the age of 60, others occurred between that age and 70, when he was left aphasic and hemiplegic after a fit.

### *Vertigo.*

Vertigo is occasionally the chief symptom in an attack of late epilepsy, when the differential diagnosis from other possible causes is sometimes difficult, and especially so when epileptic attacks and aural vertigo coexist in the same patient. Thus, a man aged 47 had a sudden attack of severe vertigo which left him deaf in the left ear, and liable to attacks of vertigo with tinnitus ; at 53 he began to suffer from fits in which he felt an indescribable feeling rising from the stomach, lost consciousness, and fell, hurting himself in falling. There was no memory of the attacks. Gowers gives several instances of this coincidence of aural vertigo and epilepsy.[14] It may be difficult to determine the nature of a single attack.

Vertigo is one of the common, and certainly one of the most distressing, nervous affections of later life. By far the most frequent form is aural vertigo. Next in frequency come the cases due to increased intracranial pressure. It is also met with over 50 as a symptom of atheroma of the cerebral vessels, in stenosis of the aortic valves, in granular kidney, in cerebral tumours, and in neurasthenia. In a few instances an association with migraine, probably accidental, was present. It occurred in this way. The patients were between 50 and 60, they had suffered from typical attacks of migraine with ocular symptoms which ceased at or before the age of 50, and then at about 55 began to be affected with severe aural vertigo. Vertigo is a rare premonitory symptom of migraine.

The form of vertigo associated with hypertension, sometimes an early symptom of contracted granular kidney, is worse on movement, and apt to occur on getting up in the morning ; the attacks are often attended by severe vomiting, which may persist for some time after the vertigo has gone. Consciousness is not affected. In one case with frequent attacks of vertigo and vomiting during two years, often lasting for two days at a time, hæmorrhage into the pons Varolii, with paralysis of the third, fifth, sixth, and seventh nerves, subsequently occurred.

## *Hysteria.*

The subject of hysteria is so vast, and there is so much difference of opinion as to what should or should not be included under it, that it is a difficult one to enter upon. Moreover, any extended notice of it here is rendered unnecessary because it was very ably treated by Professor T. R. Glynn in his Bradshaw lecture of 1913.[15] The sufferers from hysteria generally obtain some mitigation of their disorders in later life. After possibly an aggravation of their troubles during the climacteric, they experience a great improvement of health, to their own relief, and still more to that of their family. In exceptional cases hysterical manifestations persist in the same or in different forms even into old age.

The more severe hysterical affections are undoubtedly uncommon after 50. They may occasionally appear in persons who suffered from hysteria before. Because severe hysteria is uncommon in later life errors of diagnosis may be made. If the patient is a male, the true nature of his complaint is still more likely to be mistaken. Hysterical mental disorders and fits are most uncommon after 55, and in the presence of a presumed case it is necessary to bear in mind Dr. J. A. Ormerod's warning to exclude alcoholism. I have once seen a severe hysterical fit in a woman over 55, which was followed by hysterical hemiplegia, and due to the shock of her mother's sudden death.

Hysterical paralysis and contractures occur rather more frequently. I can recall two cases of hysterical paraplegia in men ; both were aged 64. Under appropriate treatment they made a complete recovery. Two instances of hysterical contracture of the leg in women, aged 53 and 51 respectively are of interest because in each case there was a possible source of auto-suggestion ; for one patient was a nurse who had chiefly to do with paralytic cases, and the other lived with a sister whose knee was permanently contracted after an accident. Both recovered after removal to hospital.

### *Neurasthenia.*

Neurasthenia cannot be regarded as a disease of later life, as the large majority of cases occur between the ages of 25 and 50. Many neurasthenics as they reach later life, though perhaps never becoming robust, yet arrive at a measure of health and freedom from morbid anxieties which has been denied them for many years. At the same time neurasthenia, though not frequent, may occur after 50 up to old age. The symptoms present no special feature except, perhaps, that vertigo is relatively more frequent and troublesome, that loss of memory may be a pronounced symptom, and that morbid fears, if present, often take the form either of fear of paralysis or of sudden death. The diagnosis of neurasthenia, always one of exclusion, requires especial care in later life, because, with symptoms resembling those of ordinary neurasthenia, it is often found that the patient has arterio-sclerosis with abnormally high blood pressure, or early signs of a granular kidney, or that the symptoms produced are due to changes in the nutrition of the brain due to disease of vessels. Such lesions exclude neurasthenia.

With regard to the traumatic neuroses, these are apt to affect persons after 50 very severely as the result of an accident, and to take the form of neurasthenia rather than of some more strictly hysterical manifestation. Here again the matter is confused by the frequent pre-existence of chronic disease of the vessels, heart or kidney, so that it may be difficult after an accident to apportion correctly the share of the illness due to nervous shock and that due to antecedent disease. The difficulty is increased by the common experience that from the gradual onset of these infirmities of advancing age the patient was unconscious of them before the accident. In medico-legal cases of elderly workmen claiming compensation after an accident—and it is only human nature for them to attribute all their trouble to it—a just decision is often extremely hard. Working men over 60, after a life of toil, generally show signs of vascular or cardio-vascular degenerative changes ; they may go on working so long as no accident or acute illness occurs, but they are in an unstable equilibrium, and if unfortunate enough to meet with a bad accident they are likely to be permanently incapacitated. The prognosis as to return to full health in traumatic neurasthenia in persons over 55 is, in my experience, not good.

### *Neuralgia.*

Between 50 and 60 true neuralgia is not an infrequent affliction. Gout, arterio-sclerosis, various cachexias, and presenile disturbances of nutrition are the chief causes. The senile and arterio-sclerotic forms chiefly affect the fifth nerve. Neuralgia may be a complication of a granular kidney, and in several cases under my care affected the occipital nerve. Occipital pain, not definite neuralgia, is sometimes a symptom of uræmia. Lapinsky has traced the neuralgia of nephritis to disease of the vessels of the nerves.

A most severe form of neuralgia in the elderly is that which follows herpes zoster. A sufferer from herpes in later life rarely escapes without subsequent neuralgia, often lasting for months. In younger patients it is quite exceptional for there to be much pain, and when present it stops with the healing of the eruption. Evans[16] suggests that this depends on a difference of cause. He thinks that a large majority of cases of herpes zoster are microbic in origin, and regards this as the essential form of the disease to which he attributes most cases occurring in children, whilst those which occur after 40 are due to causes yet undetermined. Evans states that half his cases were under 14 years of age and one-sixth over the age of 40. Head states that of 378 cases, 29 were over 40 years of age.

*Paralysis agitans*, though not a very common disease, is pre-eminently one of the period of life between 50 and 70 years. Its main incidence is narrower and lies between 50 and 65. Sir W. Gowers[17] out of 236 cases states that the onset in 51 was between 40 and 49, in 100 from 50–59, and in 60 from 60–69, altogether 211 cases. After 70 there were 10 cases. Stuart Hart[18] in 219 cases found the age of onset to be between 40–50 in 54, between 50–60 in 88, between 60–70 in 42, and none after that age. Onset over 65 is thus uncommon. The disease is therefore one of the presenile period. Its cause remains mysterious, and it is not especially associated with vascular degeneration or other bodily changes incidental to this age. Of exciting causes the most frequent is depressing emotion or sudden, profound emotional disturbance, and the other is a traumatism. In Dr. Hart's cases 27 were distinctly due to traumatism and 27 less certainly due to this cause.

## Concluding Remarks.

If from the foregoing considerations we try to get a general view of the nervous affections of the sixth and seventh decades it is clear that many nervous diseases do not occur at all, others are modified in their symptoms and course, and a few especially affect this time of life. Except for one important group of diseases it comes out more favourably in comparison with other ages than one would perhaps have expected.

It is hardly necessary to say that the lesions of the brain due to vascular disease form the exception, and although, strictly speaking, these are not primarily nervous diseases, yet from the practical point of view they are by far the most important of the nervous affections of this period, because of the great frequency of cerebral hæmorrhage and thrombosis after 50, and of their disastrous effects both as to life itself, and if that is preserved, as to future usefulness. The frequency alone of such serious diseases marks them as first in importance. Cerebral hæmorrhage, thrombosis, and hemiplegia afford a very large proportion of the sufferers between 50 and 70 from all the diseases considered in this lecture. Further, it has been shown that disease of the vessels materially affects the course of most nervous affections during this period. Since nervous tissue once destroyed cannot be restored, the prevention of vascular diseases becomes of paramount importance. How this is to be accomplished I cannot consider at length. Often the tendency to vascular disease is hereditary and beyond our powers to remedy, but apart from such cases it is certain that the chief measures to prevent degenerative changes in the circulatory system are abstemiousness in eating and drinking, care to keep efficient the organs of digestion and excretion, and regular physical exercise. The simple life may prevent, and certainly mitigates,the progress of vascular decay.

Again, the granular kidney, a disease for which, unfortunately, our treatment is merely palliative and not preventive, is the cause of a large proportion of cases of cerebral hæmorrhage. In the course of this lecture its importance as a cause of various other nervous affections has become evident.

Whilst on the one hand over-feeding has to be avoided, on the other excessive work with insufficient nutrition is also a danger. Exhaustion, over-fatigue, or over-strain are doubtless causes of such diseases as the muscular atrophies in later life. The need for moderation of former activities, both mental and physical, is a lesson that many learn too late. Defect of nutrition again may be local in the nervous system from defective supply of blood due to localised arterial disease.

Turning to those affections more purely of nervous origin, the period from 50 to 70 compares favourably with either that of childhood and adolescence or the age from 25 to 50.

In both the latter periods of life falls the incidence of the nervous diseases due to infections and intoxications from which the age after 50 is mostly exempt. The main period of onset of the hereditary and familial diseases, those included under Gowers's designation of abiotrophy, occurs in childhood and adolescence, whilst from 20 to 50, together with some abiotrophic diseases whose onset is late, the nervous affections due to syphilis and alcohol are rife. We have seen that after 50 the chances of the occurrence of cerebro-spinal syphilis are comparatively slight.

Lastly, the purely nervous diseases which are especially characteristic of this period of life are paralysis agitans, some of the combined sclerosis of the spinal cord, and certain muscular atrophies of central origin. It is possible that some of these affections owe their origin to that process of premature senescence or defective vital endurance of certain neuronic systems known as abiotrophy, and that this pathological process may occur at any age. Paralysis agitans, especially in its narrow age incidence, uniformity of symptoms, progressive character, and occasional familial tendency, suggests this mode of origin.

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# II.—GENERAL

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# ON MULTIPLE ABSCESS OF THE LIVER.

The following cases, which have been under my care during the last nine months, illustrate the difficulties in diagnosis and treatment which arise in the course of cases of multiple abscess in the liver.

Case i.—Henry John G., æt. 20, coal carrier, was admitted on January 30th, 1893, complaining of pain in the epigastrium and left hypochondrium of three weeks' duration. His family history was good; he had had no previous illness of any kind, and was temperate. Exposure to wet brought on a severe chill, which was followed by pains of a dull aching character in the back and abdomen, not increased after meals. There had been some cough with muco-purulent expectoration, and constipation; but no vomiting, fever, nor rigors. The aspect was dull and heavy, he answered questions slowly, and his complexion was of an earthy tint. The temperature was 103.4°; the tongue thickly furred, except at the tip and sides; the pulse 96, small, regular, soft, and compressible. On examination over the left side of the chest the breath-sounds were harsh and attended with rhonchi; in the axillary region from the sixth rib above to the lower border of the ribs below there was a dulness on percussion, the breath-sounds were feeble and vocal resonance diminished. The edge of the spleen could just be felt. The heart and lungs otherwise appeared to be normal.

The liver dulness extended from the fifth rib above to one inch below the lower costal margin; $4\frac{3}{4}$ inches in the nipple line. There was extreme tenderness in the right iliac fossa, but no dulness nor gurgling. The abdomen was generally somewhat tender and a little distended. No ascites. Urine normal, except for a deficient amount of chlorides.

On February 7th the abdomen was still tender and the recti muscles rigid. He complained of pain in the left hypochondrium, but the dulness here did not extend so high as at first by one intercostal space. The spleen was just felt. The liver dulness had increased, being now 7 inches in the nipple line, and its lower edge was felt to be one inch below the umbilicus. Pulse 96, soft and compressible. Four days later the patient was suffering from profuse sweats, was very much weaker and lay in a drowsy state, from which he could only be roused by speaking to him loudly. There was now extreme tenderness and decided bulging in the right hypochondriac region, and the liver dulness extended from the fourth rib to the level of the umbilicus (9 inches). On February 14th, the profuse sweats continuing and the patient's general condition being worse, an exploring needle was introduced into the prominent part of the swelling in the liver, and some blood and pus withdrawn. It was intended on the next day to make an incision into the abscess and drain it, but the patient died suddenly during the night. He had no diarrhœa nor vomiting whilst in the hospital.

At the *autopsy* the conditions present showed that an operation would have been fruitless. The liver was enormously enlarged, weighing 160 ounces. The right lobe was honeycombed by large irregular multilocular abscess-cavities, extending through it from back to front, and containing a quantity of thick highly-offensive pus. The abscesses were not enclosed by a wall, but invaded the surrounding tissues. The lobulus spigelii was similarly affected.

The omentum was adherent over the cæcum, and on removing the former the vermiform appendix was seen to be gangrenous for 2 inches, to have partly sloughed off, and to be lying in about two ounces of pus which was shut off from the general peritoneal cavity by newly-formed inflammatory tissue. The cæcum and the rest of the intestines were healthy.

Case 2.—George W., æt. 18, machinist. The patient had had a stone removed from his bladder when a boy, and fourteen months previously had suffered from an illness, stated to be "chest complaint," from which he recovered perfectly. The present illness began on February 16th, 1893, with general weakness, tremor of limbs, and anorexia. Three weeks later he took to bed with right pleuro-pneumonia, and he was admitted, on March 21st, for a supposed empyema on that side. A week before admission he had a severe attack of diarrhœa. He could lie in any position, had no pain, and no rigors. His temperature was 103°, he was pale, emaciated, and was suffering from cough with thick, frothy expectoration and from night sweats. Pulse 144, regular, soft and compressible; tongue moist, transversely fissured and covered with a thin white fur. Bowels regular. The urine contained a little albumen. No jaundice. On examination breath sounds weak, with prolonged expiration over right side and occasional moist crepitus over the left base; otherwise lungs normal. The heart was somewhat dilated, its sounds weak.

Liver dulness was six inches in nipple line, extending in front from the fifth rib above to the costal margin below; behind, the dulness began at the ninth rib. The abdomen was not distended, there was a very little tenderness in the right hypochondrium, but no ascites.

An exploring needle was inserted two inches below the angle of the right scapula but only a little blood was withdrawn, and the needle appeared to have entered the liver. On March 28th the temperature during the week had shown diurnal oscillations of septicæmic type; the patient, however, felt himself better. The heavy sweats continued; the pulse was 120, markedly hyperdicrotic, and the cardiac first sound inaudible. On April 1st, as the patient still continued very ill, and his symptoms pointed to the presence of pent-up pus, a second attempt was made to reach it, and this time successfully. The needle was inserted below the upper edge of the dulness in the sixth right intercostal space, 3 inches outside the nipple. Pus was withdrawn, and two days later my colleague, Mr. Barclay, made a free incision, and removed ten ounces of thick curdy pus. It could not positively be made out whether the pus came from an abscess in the liver, or from a localised empyema between the lung and the diaphragm. After the operation the patient felt and looked better for some days. The temperature, however, remained unaltered in range and character, and the general symptoms did not improve. In view of the extremely weak condition of the patient and of the free discharge of pus through the drainage tube it was not thought advisable to attempt any further operation. On the 11th the temperature fell, and on the 12th and 13th was markedly subnormal, it subsequently rose again. The pulse throughout preserved its extremely dicrotic character.

The patient after this grew rapidly worse, and died on the 22nd from failure of the heart.

At the autopsy the right pleural cavity contained 16 ounces of clear serum. The right lung was partly collapsed and pushed upwards by the liver. The pleural surfaces were adherent below the fifth rib in front and in the axillary region; the base of the right lung and the upper surface of the liver were adherent to the diaphragm. The liver was enormously enlarged, and together with the right lung weighed 176 ounces. It contained an abscess cavity the size of a hen's egg in the right lobe, which was further channelled throughout with small intercommunicating abscesses. The capsule was thickened, and the rest of the liver deeply congested. The drainage tube passed directly into the largest abscess, without opening either pleura or peritoneum, owing to the presence of adhesions.

The heart weighed 22 ounces; its cavities were dilated and its walls flabby. In the left auricle and in its appendix, adherent to the walls, were two polypoid masses of fibrin, quite soft, and broken down in the centre into a creamy or almost purulent consistence. The spleen weighed 14 and the right kidney 13 ounces. The pelvis of the left kidney was occupied by a large branched calculus, and the kidney substance was destroyed. A smaller calculus blocked the left ureter just below.

There was no sign of intestinal ulceration, but the mucous menbrane of the colon was injected.

The notes of the third case have been unfortunately mislaid, but the main features of the illness were the following:—

Case 3.—The patient was a seaman, aged 36, who had been some time in the tropics and had there suffered from severe dysentery. When admitted into the hospital on June 8th, 1892, he suffered from a moderate degree of fever, and from pain in the right hypochondrium. He had then the signs of right pleurisy with a small amount of effusion. During the progress of the case the fever increased, the pains in the right side became worse, and there was bulging of the right hypochondrium, with increase of the liver dulness. The patient emaciated, lost strength rapidly, and suffered from heavy sweats. About the middle of July the temperature assumed a more distinctly hectic type. Exploration of the right pleural cavity for pus towards the end of the month gave negative results, and the physical signs were such as to indicate—since the liver dulness was very much increased and the edge of the organ was felt some distance below the lower border of the ribs—either that there was a collection of pus between the diaphragm and the liver, pushing the latter downwards, or that the liver itself was greatly enlarged and the seat of an abscess. At this time an extremely tender fluctuating swelling appeared in the epigastrium, and rapidly increased in size. Pus was obtained from this swelling by an exploring needle. On the supposition that a subdiaphragmatic abscess was present, the patient was placed under chloroform, an incision made in the mid-axillary line, and exit given to a quantity of curdy pus. Afterwards the temperature fell to some extent, there was a free discharge of pus, but the man gradually lost strength and died on August 14th.

At the autopsy the right pleural cavity was obliterated by adhesions below the seventh intercostal space—two inches above the operation wound. The upper lobe of the right lung was partly consolidated ; the lower, adherent to the diaphragm, contained in its posterior part an abscess the size of an egg. In the greatly enlarged liver close to its upper surface and in the middle line of the body was a large abscess. More than twenty other abscesses varying in size from a filbert to a small orange were scattered through the liver. The opening made at the operation had passed through the adherent layers of the pleura, through the diaphragm and the anterior edge of the liver into a large abscess cavity with thickened granulating walls which lay between the diaphragm, liver, and abdominal wall. This subdiaphragmatic abscess had originated from the rupture of one of the abscesses in the liver. The mucous membrane of the large intestine presented throughout its length advanced destructive changes due to dysentery of long standing.

In none of these cases was the suppuration due to actinomycosis.

Mr. F. W. Stoddart very kindly aided me in the bacteriological examination of the pus. In the first case the micro-organism present was *staphylococcus pyogenes albus ;* in the second, *staphylococcus pyogenes aureus*, and also a streptococcus, and in the third, in addition to the *staphylococcus pyogenes*, a large bacterium was present, which he considered to be the *bacterium coli commune*. This was the case in which extensive dysenteric ulceration, the common cause or at any rate accompaniment of tropical abscess of the liver, was found. The pathological characters of the abscesses in this case did not differ in any obvious way either to the naked eye or microscopically, except for their greater size and extent, from those in the other cases. I have been unable to discover whether the *bacterium coli commune* has been frequently found in the pus of hepatic abscesses secondary to dysenteric ulceration. In tropical abscess of the liver there is most commonly a single large abscess, while in this country hepatic abscesses are almost invariably multiple and diffuse. Wilks and Moxon consider that the former begins in the same way by the formation of a number of abscess cavities which ultimately coalesce to form a large abscess. The longer duration of the illness in tropical abscess allows this to take place, whilst on the other hand the rapidly fatal termination of cases of hepatic suppuration in temperate climates does not give sufficient time. The reason of this difference is to be found in the fact that in this country hepatic abscess is usually a complication of grave acute disease and only serves to accelerate the fatal termination. Possibly further investigation may show that the more benign course of the tropical abscess is to be attributed to its association with a specific micro-organism. At any rate, the presence of the *bacterium coli commune* in the pus in this one case is interesting and suggestive.

One of the chief difficulties in diagnosis, in such cases as the above, arises from the small size and deep situation of the abscesses. When the abscess is large and single, it is, as a rule, more easily discovered, as in the following instance.

Case 4.—A navvy was admitted into hospital in September, 1892, complaining of severe pain in the right hypochondrium. During the campaign in Burmah in 1887-1888 he had three attacks of dysentery. Four months previously he was taken suddenly with a violent pain in the right hypochondriac region ; he had no rigors or vomiting. After some days he returned to work, but ever since had suffered from dull pain in the right side, from heavy night-sweats, and from great weakness and emaciation. On examination, a large, tender swelling occupied the right hypochondriac and lumbar, and extended also into the epigastric and umbilical regions. The liver dulness began above at the fifth rib, and its lower border was felt, smooth and sharp, just above the umbilicus ; it measured 5 inches in the middle line, 9 inches in the nipple, 8 and 7½ inches in the anterior and posterior axillary lines respectively. An exploring needle passed into the swelling entered the liver, and some pus mixed with blood was withdrawn. The next day the patient had three very copious loose evacuations of the bowels. He felt very much better, all pain and tenderness disappeared, the swelling diminished in size, and he therefore insisted on leaving the hospital. His temperature was normal throughout.

In this case the diagnosis was sufficiently clear. In the first patient the heavy aspect and dull mental state, the slight bronchitis, the enlargement of the spleen, and the presence of pain and tenderness in the right iliac fossa, made the resemblance to enteric fever a close one. Acute tuberculosis had also to be considered as a possible cause for the illness. After the lapse of a few days enteric fever and acute tuberculosis could be excluded ; the signs in the iliac fossa were clearly due to some perityphlitis, and those in the liver were caused by suppuration in that organ as a secondary complication. In the second case the difficulties were greater. The history of the illness led one to expect an empyema. Careful examination, however, showed the diagnosis lay between a small localised empyema between the middle and lower lobes of the right lung at the base, or simply between the base of the lung and the diaphragm, and an abscess of the liver. The streptococci found in the pus withdrawn at the operation took, as they may do, chiefly the form of a diplococcus, and, stained by Gram's method, gave the appearance of a clear concentric space around them. They thus closely resembled the *diplococcus pneumoniæ*, and if undue stress had been laid on the cover-glass preparations might have misled one, as the *diplococcus pneumoniæ* is often found in the pus from an empyema. The further course of the case after the operation gave most aid to the diagnosis, for although free drainage had been established, and there was no sign of fluid in the pleural cavity posteriorly, the septic fever continued. Thus there was some centre of suppuration present which had not been reached, and in view of all the conditions present, this was almost certain to be in the liver. The extreme dicrotism of the pulse was explained by the conditions found in the heart *post-mortem.*

In the third patient we had the previous history of dysentery to help us. The actual physical signs were those of subdiaphragmatic abscess, and these preponderated and masked those of the abscesses in the liver and right lung, which were not detected during life.

It is considered by many surgeons that an exploratory puncture in liver abscess is inadvisable, on account of the danger of an escape of pus into the peritoneal cavity. In cases of a kind similar to the preceding, however, an exploratory puncture is most valuable, if not almost necessary, to clear up the diagnosis, and to obtain reliable information as to the exact situation in which the pus can be most directly reached. It would be wise, however, in view of the possible contingencies, not to use too large a needle, and to be prepared to operate at once if pus is found. With regard to diagnosis, the ordinary signs of abscess of the liver are familiar to everyone, and it is needless for me to recapitulate them. I propose therefore only to consider the chief points in the differential diagnosis of the more obscure cases, and especially of those in which there is more than one abscess, and no one of any very great size.

The first step then, and it is sometimes not a very easy one, is to ascertain whether abscess of the liver is the condition present. Abscess of the liver has to be distinguished from abscess in the lower lobe of the right lung, from certain cases of localised empyema, from a collection of pus between the liver and diaphragm, from perihepatitis, from a suppurating hydatid cyst in the liver itself, and from an abscess in the abdominal wall. The last condition we need not discuss, and a suppurating hydatid cyst could hardly be distinguished from hepatic abscess due to other causes. We may also eliminate those cases in which the presence of a large abscess in the liver betrays itself by unequivocal symptoms which are easily recognised. One must bear in mind that a solitary hepatic (tropical) abscess may remain entirely latent, and that the temperature may remain normal, as in Case 4 above. This appears to be an exceptional occurrence, and examination would probably detect in such cases, as in that one, a large localised swelling of the liver which would be assigned to its proper cause. Such a case might present difficulties of its own in diagnosis, which, however, would not be of the same kind as those in the group which we now pass on to consider.

These are the cases of diffused suppuration, or occasionally of deep-seated solitary abscess, attended with a more or less uniform enlargement of the liver, which predominates as a rule in the right lobe, in which there is often great difficulty in recognising the exact conditions present. For instance, a patient suffers from pain in the right hypochondrium, from more or less uniform enlargement of the liver, with extension of hepatic dulness both upwards on to the chest and downwards on to the abdomen, from high fever of hectic type, possibly from rigors, from rapid emaciation, prostration and heavy sweats. It may first of all be difficult to decide whether such an enlargement of the liver dulness is due to actual increase in size of the organ itself, or to its displacement downwards by a collection of pus above it. Abscess of the lung will most probably be found in a patient with a history either of some chronic lung affection, or as a rare sequel to pneumonia in a person of intemperate habits or broken constitution, and will be attended with the expectoration of pus, if, as is generally the case, there is a communication with a bronchus. In both this affection and in empyema the more typical symptoms of abscess of the liver, tenderness in the right hypochondrium, the peculiar dull pain and sense of weight there, and very heavy sweats will be absent. Displacement of the heart's apex to the left, if extreme, is in favour of empyema, but a moderate degree of displacement may occur in abscess of the lung or liver. Further, in some cases of the obscure kind now under consideration, the enlargement of the liver dulness in a downward rather than in an upward direction into the chest, may point to the presence of abscess of the liver; in others no such help is afforded by the direction of the extension of dulness. Nor is the decubitus of diagnostic significance except where the abscess is a large one.

In cases of subdiaphragmatic abscess the pus may come to the surface during the course of the illness (as in Case 3) and its situation be clear. Before this occurs the points in the diagnosis are—bulging of the right hypochondrium, displacement downwards of the liver as a whole rather than enlargement of any particular part of it, the presence of fever of septic type, and the history of some complaint liable to give rise to such a complication such as gastric or duodenal ulcer, suppuration about the right kidney, or mischief in the lower part of the right chest. Moreover, a subdiaphragmatic abscess may be a secondary consequence of abscess of the liver, as in Case 2 above.

An exploratory puncture may enable us to determine the exact situation of the pus. Sometimes even with this aid we cannot positively decide whether the abscess is in the liver, is above the diaphragm, or subdiaphragmatic; even when an opening has been made and free drainage established there may still be a doubt at the time of operation. In such cases the subsequent course of the illness is the most reliable guide. For in empyema, in subdiaphragmatic, and in solitary hepatic abscess, the establishment of a free discharge for the pus will result in the subsidence of fever and an improvement in the general condition of the patient. Should there, however, be little or no improvement after the operation, in these respects, we may conclude that we have to do with multiple abscesses of the liver. Exception must possibly be made for a localised empyema of tuberculous origin, but the presence of tubercle will be betrayed by other signs. In such cases the question of further operation must be decided according to the conditions present in each particular case. Study of the foregoing cases shows that by the time we are enabled to decide that the patient is suffering from multiple abscess of the liver the destructive changes in the organ are too profound and too extensive to be capable of cure and therefore it would be useless to attempt any further interference. The exploratory operation must often be undertaken in uncertainty as to the exact condition present, for, as has been pointed out, the cause of the illness subsequently to operation may be the first certain indication that there is more than one abscess present. Of course there is always the chance that we may be fortunate enough to drain more than one abscess by the first opening, and so occasionally enable the patient to pull through, and by giving exit to the pus, considerable relief to pain is afforded, but the nature of the disease does not seem to make more than one operation desirable, at all events so long as pus flows through the drainage tube.

Multiple hepatic abscess thus tending to a fatal termination, it becomes very important to be able clearly to distinguish this condition from the solitary abscess, which may be cured by operative measures. On what signs are we to rely for the distinction? The history of the illness is most important: in multiple abscesses the disease runs an acute course, in tropical abscess a long one, and it would further seem correct to state that if abscess of the liver occurs in a person who has not resided in the tropics nor suffered from dysentery, the very great probability, or practical certainty, is that there is more than one abscess present, and that these are diffused through the liver. Further, if the pathognomonic signs of a large abscess are absent, that is in favour of the existence of several abscesses rather than of a single large one, which, from its deep situation or other causes, has not given rise to the usual signs.

One brief remark in conclusion with regard to prophylaxis. Suppose that we are attending a patient who is suffering from enteric fever, dysenteric ulceration of the bowels, or some similar intestinal complaint, and that he is taken with pains over the liver, rigors, and a fresh rise of temperature, we should bear in mind the somewhat rare complication of hepatic abscess in such conditions, and endeavour to prevent it by dealing with the source of infection by promoting intestinal antisepsis. This may be done by the administration of naphthol, salol, salicylate of bismuth, or chlorine water, in efficient doses.

# THE TREATMENT OF ENTERIC FEVER.

THE proper treatment of a fever which, as in the case of enteric fever, is due to a specific organism consists in the administration of some substance which will destroy or check the growth of the organism, and neutralise or render inert its toxic products when they have already gained entrance to the system; but unfortunately we are not at present in possession of such a remedy, although the progress on these lines that has recently been accomplished in dealing with some other of the specific fevers, and the efforts already made in enteric fever itself, lead us to hope that we may have one in the near future. Then there will be no scope for discussion on the treatment of enteric fever, or only the very limited one afforded by the investigation of the best mode of administration of the therapeutic agent.[1]

Failing true specific treatment, our efforts must then at present be concerned, since we cannot meet and destroy the virus by its proper antidote, with the best means of sustaining the patient's strength, of increasing and maintaining his powers of resistance against the toxic products absorbed from the intestine; of reducing fever when this is excessive in itself; of hindering the fermentative processes going on in the intestine, and thus preventing as far as possible the absorption of poisonous products which can so readily take place through the broken surface of the ulcerated intestinal wall; and of combating those complications which so frequently arise in the later stages of the disease and are in themselves directly dangerous to life. I propose to deal chiefly with the best means of maintaining the general well-being, of treating fever, of preventing excessive fermentation processes in the intestines, and of dealing with the most serious complications.

With regard to the general management of the patient and the hygienic measures to be adopted I need say little. Absolute rest with a fluid, easily assimilable, and nourishing diet are of course essential. Milk, which may require to be modified in different ways to suit individual patients, will be generally accepted as the best food, with the addition of barley-water, beef-tea, and meat extracts ; I allow in addition the beaten-up yolk of an egg, once or twice in the twenty-four hours, but I think that the use of more solid food, which has been recently advocated in order to obviate the extreme weakness of the late periods of the illness and to shorten the period of convalescence, is not at all advisable. It must largely increase the risk of perforation and hæmorrhage, those two most formidable complications.

As to the use of alcohol, the guide to its administration is to be found in the state of the pulse. Alcohol should be given freely when there is any sign of heart-failure, reducing or dropping the dose again when the threatening symptoms are averted. It is indicated in states of quiet delirium, when collapse is threatened, and in insomnia ; a sufficient dose of alcohol at bed-time often ensures a good night. It is also of service in the apyrexial interval before solid food can be allowed, as it mitigates to some extent the pangs of hunger, besides being a useful stimulant at a time when the action of the heart is often weak.

Perhaps the chief differences of opinion lie in the estimation of the relative advantages of the expectant, antipyretic, and antiseptic methods of treatment, or of the combination of the two latter. Taking first of all antipyretic treatment, it is to be borne in mind that in treating fever we deal only with a symptom and not with the disease, and that a certain degree of pyrexia is considered by many to be not only not injurious, but beneficial to the organism in hindering the growth and development of the virus.[2] But although opinions may differ as to the utility of reducing pyrexia as an end in itself, it is generally held that a long-continued high temperature is injurious to the organism, and this view is based on the *post-mortem* changes found in the organs as a consequence of persistent high fever, which therefore calls for active interference. What mode should this interference take? "The researches of Zuntz show conclusively that only the reflex apparatus for regulating temperature *which is always at work* is that which governs the loss of heat at the surface."[3] This would indicate that the best and safest method of reducing pyrexia is that of abstracting heat from the surface by the application of cold, and clinically this is conclusively shown by the good effect of cold baths in hyperpyrexia.

The use of antipyretic drugs to reduce fever, phenacetin, kairin, antifebrin, antipyrin, *et hoc genus omne*, from which a few years ago so much was anticipated, but which has now been practically given up, is fraught with danger, because of their depressing action on the nervous system and the circulation, and because of the reduction of the flow of urine and consequent elimination of toxic products; whilst their effect on the temperature is often to lower it too suddenly, and also to be too transient. The mortality of cases in which treatment by these antipyretic drugs is carried out is from 12 to 16 per cent., that of cases treated by cold baths 6 to 8 per cent.; a result which speaks for itself.

If then it is allowed that the application of cold to the surface is the best measure to take for reduction of fever, how can it be most effectually carried out? There is no doubt that by far the most effectual method is the cold bath treatment. Now in employing cold baths we are not open to the reproach of treating merely the symptom, pyrexia; for Roque and Weil claim to have shown that in "typhoid fever left to itself the toxic products manufactured by the bacillus and organism are eliminated in part during the illness. The urotoxic coefficient is double the normal, but this elimination is incomplete and it is only completed during convalescence, for the hypertoxicity continues for four or five weeks after the cessation of the fever. In typhoid fever treated by cold baths the elimination of toxic products is enormous during the illness. The urotoxic coefficient is five or six times the normal. The hypertoxicity diminishes as the general symptoms mend and as the temperature falls, so that when the period of pyrexia ends and convalescence sets in the elimination of toxins has ceased."[4]

Further, apart from the question of treating pyrexia, the advantages claimed for the bath, and, so far as my experience goes, justly claimed, are[5] that (1) the intellect becomes clearer, the stupor lessens and the muscular twitchings disappear; (2) there is a general tonic action on the nervous system and particularly on the heart; (3) the insomnia is lessened, the patient usually falling asleep after each bath; and last and most important, the mortality is reduced. Thus Dr. Dreschfeld quotes:[6]

| | | | | |
|---|---|---|---|---|
| Drasche (Vienna) as finding a reduction from | | 16.2% | to 9.3% | mortality. |
| Tripier and Bouveret (Lyon) | ,, | 25.0% | ,, 7.5% | ,, |
| Osler (Baltimore) | ,, | 21.8% | ,, 7.4% | ,, |
| Thompson (New York) | ,, | 19.0% | ,, 7.0% | ,, |
| Vogl (Munich Garrison) from | 1841–1860 mortality | 21.0% | expectant treatment. | |
| | 1860–1875 ,, | 15.2% | *partial* bath treatment. | |
| | 1875–1882 ,, | 6.5% | bath treatment. | |

Dr. F. E. Hare[7] gives the following striking statistics of the cold bath treatment of enteric fever at the Brisbane Hospital: The mortality was lowered from 14.5 per cent. to

7.5 per cent. The number of patients was 1,902. Mortality under bath treatment—

| | | | | | |
|---|---|---|---|---|---|
| From perforation, | 2.9%. | Before bath treatment, | | | 2.9 %. |
| ,, | hæmorrhage, 1.2%. | | ,, | ,, | 1.88%. |
| ,, | other causes, 3.4%. | | ,, | ,, | 9.73%. |

The death-rate per number of patients affected with enteric fever is still for England the same that Murchison gives, 17 per cent.;[8] at a large London hospital it was 26 per cent., 12 per cent., and 11.2 per cent. for the last three years respectively. Dr. Dreschfeld concludes that the evidence appears to be conclusive that the hydropathic treatment strictly carried out has considerably lessened the mortality; and if I bring forward facts already familiar, my excuse must be that in view of this lowered mortality the bath treatment has not sufficiently come into use in England. I do not think the bath necessary for very mild cases in which the highest range of temperature is from 102° to 103°: for these sponging is sufficient. I began to employ the bath treatment systematically about two and a half years ago in consequence of the favourable reports published of it, and of the fact that it is difficult to reduce the temperature sufficiently by sponging, and that the effect produced does not as a rule last long. Before this I employed cold sponging in all my cases, sponging being carried out every four or five hours as a matter of routine, except where the case was a very mild one, when it was done less often. In all others than mild cases the bath is employed. The advantages over sponging are: (1) it has greater and more prolonged effect; (2) the temperature can always be reduced by it, whereas sponging may fail; (3) the beneficial effect on the nervous and vascular systems is much more marked; (4) if properly carried out it does not necessarily involve more movement of the patient.

This last statement, which is obviously one of practical importance, may seem unlikely; and to ensure the bath being properly given with the least possible movement of the patient, if he is an adult of about the average weight, three persons will be required to lift him into the bath: if the patient is very light, two nurses can easily lift him in and out. Several times I found that the temperature did not fall in the bath, and once or twice even went on rising; but, on taking the temperature half an hour afterwards, it had invariably fallen. On only one occasion the bath failed to reduce a high temperature of 105°, and then the time of fifteen minutes was not exceeded on account of the patient's pulse being very weak. On one occasion only some collapse was produced; but then the patient was kept in the bath too long. The effect on the pulse when this is very rapid and feeble is, as a rule, good, the pulse becoming fuller and slower afterwards. I need not enter into the details of carrying out the bath treatment, as they are now well known. The bath seems especially valuable in those cases in the third and fourth week in which the temperature shows a decided tendency to rise and to remain at a high level; the effect, in cases with pronounced nervous phenomena, and with insomnia, and, as said above, on the circulatory system, is, as a rule, very satisfactory. In any case of enteric fever with a high temperature range, I should feel that without the bath the best was not being done for the patient. If it could not be carried out, I think sponging in ice-cold water or an ice pack is the most efficient substitute. Another measure, but less efficient, is the suspending of small pails of ice from a cradle with the patient lightly covered. The most important contra-indications of the bath are hæmorrhage in the later stages, peritonitis, perforation, and possibly myocarditis. Neither pneumonia nor nephritis precludes its use. An interesting case of enteric fever with the latter complication was recently published,[9] in which Dr. Tyson showed that the amount of urine and quantity of urea excreted increased under the use of cold baths.

On the other hand, it is useless to deny that there are considerable difficulties in carrying out the bath treatment, especially when the patient is a large, heavy person. In institutions it is more easily carried out than in private, although in the houses of the well-to-do, where one has plenty of assistance, it can be managed without much difficulty. One objection is the great dislike that many patients have of it, the dread that it may excite in a very nervous patient may have a prejudicial effect on the course of the illness and prevent its employment. I have had patients, however, who liked it, because they felt refreshed by it. I have heard of a few cases in which the use of the bath was discontinued on account of its being followed by depression of the circulation and excessive cyanosis : but I have not met with any instance myself in which, when carefully carried out, the effect on the heart and circulation was otherwise than beneficial ; and the absence of dicrotism in the pulse is noticeable in cases treated on this plan. The improvement in patients who are lying in a state of stupor or semi-coma is also remarkable, and not attained by other modes of treatment. Lastly, it is of great advantage to have a nurse who has had experience in carrying out the bath treatment : this is, in my opinion, a very important point.

I believe that a further means of treatment of value lies in the administration of intestinal antiseptics. Although we cannot expect by the use of intestinal antiseptics to destroy the typhoid bacilli which, by the time the treatment has begun, have already entered the intestinal wall, and reached the glands and other internal organs, we may hope to hinder the action of other organisms in the intestinal contents, whose growth is favoured during the course of enteric fever, and thereby to diminish fermentative action, undue distension of intestines from products of fermentation, and to neutralise or hinder the absorption of the poisonous products through the ulcerated surface.

Under this head I include the administration of calomel, a measure of undoubted value in the early stages. If a case is seen before the seventh day it is well to begin treatment for two or three nights in succession with a dose of gr. iij.—gr. v. of calomel. It has been claimed that the course of the fever is thus rendered milder and the duration shorter. Such a dose will usually have a mild purgative action, and thus get rid of a certain amount of toxic material, and is in addition a powerful antiseptic, for it has been shown experimentally that calomel kills bacteria, hinders the butyric acid fermentation and the formation of indol and skatol, the products of decomposition in the intestines. But for continued use some other substance must be sought, which to be an efficient antiseptic, and at the same time innocuous to the patient, should have the following properties: It should hinder the development of bacteria and neutralise their products, and at the same time not interfere with the digestion of food; it should be insoluble, so that it will not be absorbed, and thus pass more or less unchanged through the alimentary canal, so as to exert its antiseptic action throughout the greater part of it. There is no substance known at present which fulfils all these indications; but of those that we have I believe the naphthols most nearly do so. They are nearly insoluble in water, and have at any rate no injurious effect on the organism. In a former paper [10] I showed that although $\beta$-naphthol in a proportion as large as would be present in the stomach during its medicinal administration delayed the digestion of meat, it had no effect on the digestion of milk by artificial gastric juice, and would therefore not be prejudicial in this respect in the treatment of typhoid fever.

Drs. N. Surveyor and Vaughan Harley state [11] with regard to the antiseptic power of β-naphthol, from test-tube experiments, that both β-naphthol and bismuth subnitrate have the power of preventing or hindering the growth of various micro-organisms, and β-naphthol is the stronger of the two in some cases; the safest proportion for β-naphthol being 8—1000, and for bismuth subnitrate 10—1000. Further experiments on the number of colonies present in different parts of the intestines of dogs fed on the same diet showed that bismuth subnitrate is more powerful as a germicide than β-naphthol when large doses are used, but internally β-naphthol appears to act better than bismuth subnitrate. The reason for this discrepancy they find in the fact that although the latter is the stronger antiseptic, its value is lowered on account of its constipating property.

Mr. F. W. Stoddart kindly made some plate cultivations for me from the stools of patients with enteric fever who were being treated by hydronaphthol and bismuth β-naphthol. Although from the complicated nature of the conditions present it is impossible to draw any conclusions from the number of colonies present, which were enormous, there was one marked difference from stools of enteric fever patients not treated by antiseptics. This difference lay in the absence of colonies of liquefying organisms, which did not appear for fifteen days in one case. Mr. Stoddart tells me that these liquefying organisms are the most sensitive to the action of antiseptic agents, and so far as it goes this affords evidence that the naphthols have some antiseptic action in the intestinal contents. One case was treated by baths, the other not; there was no obvious difference between the character of the cultivations.

If any continuous efficient intestinal antisepsis is to be produced, the dose must be frequently given in order to keep up a constant effect: I usually give gr. iii.—v. bismuth β-naphthol or hydronaphthol every 2½ to 3 hours, day and night. Unfortunately the naphthols leave a pungent after-taste; this is least with bismuth $\beta$-naphthol: the dose is given floated out on a little milk. Clinical evidence shows that bismuth $\beta$-naphthol is the most useful, it has very little taste and is the most effective in checking diarrhœa. Under its action the stools lose their offensive odour and become dark in colour. The diarrhœa of enteric fever is soon checked by its administration, but if it should continue a very efficient combination is formed by the addition to each dose of gr. i.—gr. ii. of Dover's powder. Besides the marked effect on diarrhœa and odour of the stools, hydronaphthol and bismuth $\beta$-naphthol have a most important action in preventing excessive abdominal distension; in fact, this symptom, which under former methods of treatment was often so troublesome, is as a general rule absent when these antiseptics are given. This seems to me an important result and a considerable element in the successful management of enteric fever, for excessive distension is dangerous in many ways. First, by favouring the occurrence of the most formidable and fatal complication, perforation of the intestine, which according to Murchison occurs in nearly one-fifth of the fatal cases, and 1 in 33 of all cases. Then when the heart's action is weak it must be further embarrassed and the descent of the diaphragm impeded by the pressure from over-distended intestines,

In my former paper,[12] besides the above advantages, I further claimed for the use of the naphthols that the tongue remains cleaner, relapses are less frequent, the duration of the disease is shorter, and the infection to others less probable. More extended experience has, however, shown that with the exception of the tongue being cleaner, no advantage in the other respects is obtained over other methods of treatment.

Other antiseptics that have been advocated are carbolic acid, liq. hydrarg. perchlor., salol, betol, benzonaphthol, and chlorine. It is difficult to use the first two in sufficient doses without running the risk of producing toxic effects. Salol is efficient, but has the disadvantage of giving rise in the intestine to salicylic acid, which passes out by the kidneys and is probably irritating, and may be injurious to them when excreted in large doses for some time. Benzonaphthol seems to me less useful than the others.

It is difficult to form an estimate of the effect of the antiseptic treatment on the mortality. Dr. Dreschfeld states[13] that at the Monsall Fever Hospital, where the mean mortality is about 17 per cent., the mortality fell during one year when this treatment was extensively used to 13 per cent.

With regard to the treatment of special symptoms or complications a few words may be said. Small doses of phenacetin and caffeine were found to be very efficacious in relieving the headache of the early stage when this was severe. When there is much delirium the application of cold water to the head by means of Leiter's tubes is often effectual: an increase in the amount of stimulant taken is generally necessary, and a dose of morphia or chloral and bromide may be required.

The treatment of abdominal distension and of diarrhœa has been already referred to: should the latter not be controlled by the measures there recommended, a starch and opium enema generally stops it. For constipation I have always found small enemata of soap and water, or of soap and water mixed with olive oil, sufficient. Insomnia is generally relieved by bathing or an extra dose of stimulant at night; if more is required, a dose of morphia is in my experience the best remedy. Close attention to the state of the heart and pulse is most important in the later stages of the fever: should any threatening of heart-failure appear, the patient should at once be put upon digitalis; and if evidence of heart-failure is actually present, hypodermic injections of strychnine are the most effectual remedy. Caffeine is also extremely valuable in this condition, it may be given by the mouth, or in case of pressing need injected subcutaneously. Caffeine and strychnine may both be continued for some time till the danger is past with beneficial effects. I have also found hypodermic injections of spartein sulphate (gr. ½) of great service when one wished to produce a rapid effect upon the heart. Of course when digitalis is given for any time its effects need to be carefully watched. For hæmorrhage, besides the ordinary measures in the way of regulation of food, application of ice to the abdomen, ice to suck, and administration of morphia, turpentine in capsule in doses of 10—20 minims every 4 hours has given me good results, or lead and opium may be administered. If the post-hæmorrhagic anæmia is extreme, subcutaneous or intravenous injections of saline fluid may be required. One boy, in whom after a large hæmorrhage in the first week the extremely anæmic condition gave rise to anxiety, seemed to derive benefit from marrol; a preparation of the red marrow of the ox.

I may perhaps give a brief account of the cases under my care since March, 1893, which were treated on the above plan, though the number is not a large one.

The number of cases was 70, of these about 30 were treated before I began to use the bath. In these latter, cold sponging was carried out every 4 to 6 hours, except in the mild cases, when it was done less often. Of the others, sponging was resorted to in very mild, the bath treatment in the moderate and severe cases. The cases were of all grades of severity, as is roughly shown by the temperature records: in 41 cases the temperature at some time exceeded 104°, in 15 it reached 105°, in 4 106°, and in 1 107°: of the last 5, 4 recovered.

I have omitted 3 fatal cases; namely, one patient who had been ill three weeks before entering the Hospital and in whom perforation occurred the day after admission, another who was also the victim of advanced pulmonary tuberculosis, and a third who died of diphtheria when apparently safely through the attack of typhoid. On the other hand, I have included a patient who died of hæmorrhage four days after admission, and had been ill outside the Hospital for 21 days with insufficient attendance; the other fatal case of hæmorrhage was also ill with fever a fortnight before he came into the Hospital, and, further, several of the patients had been ill for periods varying from 10—21 days before admission, during which time they had either been getting about, or had been inefficiently nursed, circumstances which materially add to the gravity of the prognosis.

Of these 70 cases, 5 died,—2, mentioned above, of hæmorrhage, 2 of perforation, 1 during a severe relapse in the sixth week of a protracted attack, and the fifth of heart-failure: this last was a very bad case, the patient being admitted in a state of violent delirium with large subcutaneous hæmorrhagic extravasations on the right buttock and both heels, and a petechial eruption on the skin.

The mortality is thus 7.1 per cent. The duration of pyrexia in Hospital was 17 days; there was diarrhœa in 40 cases; hæmorrhage in 6, which was fatal in 2; a true relapse occurred in 9 cases, the average duration was 13½ days; there was lobar pneumonia in 2 cases; thrombosis of the left femoral vein in 1, and of both femoral veins in another case.

It seems to me that until we have at our disposal a remedy which is capable of destroying the typhoid bacillus and neutralising its toxic products, no form of treatment is likely to reduce the death-rate below 6 or 8 per cent. in a fever which runs such a long course as enteric fever, exposes the patient to so many and such formidable complications, and exercises so great a drain on the patient's strength; and that the combined treatment by some form of intestinal antiseptic—innocuous to the patient in other ways—and by the employment of cold baths is at present the best available one. The low mortality now an established fact for the bath treatment is, in comparison with the results of other methods of treatment, a sufficient argument in its favour. Lastly, there is a striking improvement in the appearance of the patient treated by intestinal antiseptics and baths: the "typhoid aspect" is far more seldom seen, and never in so pronounced a degree as under the "expectant" plan; the pulse is better, with less tendency to dicrotism; the tongue cleans early and remains moist; there is less of the low, muttering delirium and of the trembling and twitching of the muscles; whilst the mind remains clearer, and sleep is more refreshing. In the absence of a specific remedy, all measures must fail in a certain proportion of cases; the object must be to make this unavoidable percentage of deaths as low as possible, and I believe that treatment directed on the lines above described is that which at present conduces most to this result.

## REFERENCES.

[1] With regard to the prophylaxis of enteric fever attempts have been made by Wright and Semple and Pfeiffer and Kolle to "vaccinate" against enteric fever by injections of emulsions of Agar cultures of typhoid bacilli in which the bacilli have been killed by heating to 60° C. for five minutes, based on the view that Widal's serum-reaction is a sign of immunity. The process is free from risk, but is still on its trial.

[2] The *Practitioner*, 1897, lix. 625, quotes some interesting experiments on this subject which have recently been made. Loewy and Richter (*Arch. f. path. Anat.* [etc.], 1896, cxlv. 49) raised the temperature of rabbits, by puncture of the heat-regulating centre in the corpus striatum, sometimes as high as 107.5° F. The temperature remained high for months, or if it fell, could be raised again by a fresh puncture, and the rabbits were well in other respects. They were inoculated with pneumococci and with the organisms of fowl-cholera, swine-erysipelas and diphtheria, and the course of these infections was always favourably influenced. None of the animals died sooner than the control animals, and some survived what should have been a fatal dose. Fischl (*Prag. med. Wchnschr.*, 1897, xxii. 49, 63) on the other hand found that when the temperature of rabbits was artificially lowered to 10° C. they became more susceptible to injections of cultures of pneumococci and died more readily than the control animals.

[3] Burdon-Sanderson in *A System of Medicine*, edited by T. Clifford Allbutt, 1896, i. 159.

[4] *The Means by which the Temperature of the Body is Maintained in Health and Disease*, by W. Hale White, 1897, p. 73.

[5] *The Principles and Practice of Medicine*, by W. Osler, 1892, p. 35.

[6] *A System of Medicine*, edited by T. Clifford Allbutt, 1896, i. 845.

[7] *Practitioner*, 1897, lix. 254.

[8] Dreschfeld, *loc. cit.*

[9] *Amer. Jour. Med. Sciences*, 1897, cxiv. 290.

[10] *Practitioner*, 1890, xlv. 1.

[11] "The Action of Beta-Naphthol and Bismuth Subnitrate as Intestinal Antiseptics," *Brit. M. J.*, 1895, ii. 1483.

[12] *Loc. cit.*

[13] *Loc. cit.*, p. 846.

# THE RELATION OF MEDICINE TO THE NATURAL SCIENCES.

If there is one feature more than another which distinguishes the civilisation of to-day from that of former ages, it is the rapid rise out of comparatively insignificant beginnings of the vast and imposing structure of modern science. The latter part of the nineteenth century especially is characterised by the remarkable developments that have taken place in the natural sciences and in scientific methods of thought, and it is safe to assert that of the learned professions none has advanced more rapidly, or shown greater changes in both its theory and practice, than medicine.[1] To no other profession has so wide a vista of future extension been opened up.

This fortunate condition we owe to the great advance of modern science, which has extended the scope of the healing art, widened its interests, and brought it into touch with almost every form of scientific activity. We have only to consider modern surgery in order to realise the great gulf, the absolute difference in kind, which divides the medicine of the present day from that of even so recent a time as one hundred years ago. Science has entered so fully into our lives, has become such an intimate part of them, and we have come to regard this so much as a matter of course, that we rarely stop to think over the great changes that it has wrought.

The practice of medicine and surgery now consists essentially of the application to our art of the discoveries made in physics, chemistry, electricity, and biology. We might define present-day medicine as science applied to the study and treatment of disease. Not only is this true of practical methods, but thought and opinion have also been modified to an extent that we hardly realise. It is difficult to put ourselves into the mental attitude of our predecessors towards the problems of life, but I shall probably be correct in saying that the theory of evolution has effected no less striking a change in philosophy, in our views of life, and of the nature of the universe, than applied science has in our daily practice. We may, as Dr. Payne pointed out in his Harveian Oration for 1896, regard this modern advance in scientific knowledge as the latest of the several revivals that have occurred in preceding ages of the Greek spirit of inquiry at first hand into the laws of nature. In our own profession this principle of direct observation and experiment was first acted upon by Hippocrates and the Hippocratic physicians, and is exemplified in the remark of Aristotle, that " of doctors those who practice their art in a scientific spirit begin the study of medicine by working at natural science." The history of medicine is one of periods of inactivity, of torpor and stagnation, alternated with periods of advance. These latter have always been marked by a recrudescence of the Greek method of experimental investigation into natural phenomena. The periods of stagnation have equally been remarkable for absence of direct observation, and for wealth of theory and stereotyped systems of medical practice. More than once, as for instance in the days of Galen, then again in the time of the circulation of the Arabian treatises on medicine, imperfect embodiments of the Greek spirit as they were, and, later still, when at the opening of the Renaissance large numbers of the original Greek manuscripts were brought into Italy, we owe a period of progress to the rediscovery and reperusal of the Greek masters themselves, and are thus directly indebted to their writings for a fresh step forwards. Far more important, however, than the actual facts and observations contained in their works is the debt we owe to them for laying down, once for all, the true principles on which alone a sound advance could be made. The discoveries of modern medicine and the enormous strides that it has made are not chiefly to be attributed to the invention of any new principle on which work should be based, but rather to the application to present-day problems of principles already established from of old, by the aid of the greater wealth of those appliances, which we owe to the infinitely greater extension of the allied sciences. Perhaps the new principle which most concerns our art, and which, although dimly foreseen in some speculations of the ancient philosophers, was never realised by them as a working force in biology, is that which underlies the doctrines of evolution and advance by natural selection. It is somewhat strange that this, one of the greatest contributions of modern science on its speculative side, has so far borne little fruit in the field of medical research. We can hardly say that the Darwinian theories have been worked out in relation to disease. This is partly due to the complex nature of the problems involved, partly also, I think, to the insufficient biological training which the majority of doctors receive. Consequently the purely biological aspect of medicine receives little consideration, although there must be much to be learnt in this respect, which would greatly help to elucidate the problems of disease as it affects different races.

The story of the relation of medicine to science in former ages, down, we may say, to the modern era, is briefly a history of the gradual rise and growth of science out of medicine through the labours of the medical profession. One of the chief glories of the history of medicine lies in the many important discoveries that have been made in pure science by medical men. I do not here allude to those who were medical men by accident, as it were, and who soon abandoned their profession for more congenial occupation in the natural sciences—on such grounds we might as well claim poetry as a product of medicine because Keats was a doctor—but to men who, though engaged during most or the whole of their lives in the arduous pursuit of medicine, yet kept alight the torch of science and passed it on to their successors, leaving us for emulation their great example.

This condition of things was partly a consequence of the fact that down to the modern era men mostly studied the natural sciences as an approach or introductory study to medicine, as is inferred in the sentence of Aristotle I have already quoted. In Greek times there was nothing exactly corresponding to modern science; the natural sciences comprised descriptive botany and biology, with a certain amount of anatomy founded on dissections of animals, and a still smaller knowledge of physiology derived from the apparent uses of organs as shown by anatomical observations. Chemistry was unknown, and physics also in the modern sense of the term. The Greek study of the laws of physics, although in some directions it carried them far—Democritus, for instance, went very near to anticipating the atomic theory—was chiefly concerned with transcendental or speculative inquiries as to the nature and origin of matter, and as to the structure of the universe. These systems of physics and correlated metaphysical speculations did not greatly influence medicine, so that it escaped in these times an overloading with theory. Hippocrates and his followers kept to the sound paths of anatomical, pathological, and clinical observation. Hence medicine in its early days avoided the fate which awaited it in the Middle Ages, when it was divorced from experiment and observation, and held fast in the bonds of tradition and the preconceived theories of the schools.

During long subsequent ages medicine preserved the same relation to such science as was known, and with few exceptions the workers at science were medical men. In the early Renaissance the renewed study of science was the outcome of the revival of Greek learning, which arose from the passage into Italy of teachers from Constantinople, carrying with them manuscripts of the Greek writers on natural science. The scientific revival at this time accordingly followed the lines of the ancient Greek authors, and was practically confined to biology and anatomy. However, the study of anatomy, and of a certain amount of physiology in correspondence with it and derived mainly from anatomical observations, was carried by the aid of fresh investigations to a higher level than had ever been previously attained. Pathological observations on the dead body began to be made again, and the relation of *post-mortem* changes to symptoms during life to be traced out. Soon afterwards came the great discoveries of Harvey, who started anatomical and physiological researches on the right path, which they have ever subsequently followed, by insisting upon the necessity and demonstrating the value of the experimental method of inquiry, and incidentally almost at once placing anatomy and physiology on a sounder basis.

Hitherto, as we have said, medical progress had been wholly on the ancient lines of biological study. Long before this, however, the beginnings of the mystical study of alchemy in Alexandria had foreshadowed the rise of a new science, that of chemistry; but it is not until Paracelsus (A.D. 1493) that medicine was at all influenced by the beginnings of this science. Fantastic charlatan as in some respects he was, Paracelsus was the first to attempt, however imperfectly, to apply the then scanty knowledge of chemistry to the practice of medicine, and was the precursor of that iatro-chemical school which subsequently attained to so great an influence. The views of Paracelsus regarded diseases entirely in their relation to drugs, and had thus nothing in common with the traditional Galenical teaching of medicine, or with that of the anatomical school which succeeded it.

Sir Michael Foster points out that alchemy did not affect medicine earlier, because the alchemists who sought for the philosopher's stone and the elixir of life were not, as a rule, doctors, and, moreover, often carried on their work in solitude far apart from medical schools and universities. Hence "a certain antagonism arose between this nascent science of chemistry and the older biological studies which formed the basis of medical education. The latter was the heritage of a long-established, powerful profession; the former was the product of amateurs, of the efforts of scattered independent workers, and as such was despised by professional men."[2]

Through this long period, then, science is mostly in debt to medicine for any advance that was made, and for some time still this remains true, but to a progressively less degree, as we now come with the origin of the sciences of physics and chemistry in the first part of the seventeenth century to the beginning of the modern era, in which the bulk of scientific work ceases to be done by medical men.

During the whole of the seventeenth and eighteenth centuries, however, considerable contributions to science continued to be made by physicians labouring side by side with workers in pure science. Now science begins to repay her debt to medicine, and to repay it a thousandfold, so much so that we shall find that in future we have to look to science for the source of the chief advances in our art. In connection with the early history of physics and its application to physiology the illustrious names of Galileo, Descartes, and of Borelli, the friend of Malpighi, cannot be passed without mention, and in chemistry that of Van Helmont, especially in relation to his work on fermentation. The new discoveries in physics and chemistry enabled these sciences to be employed in the elucidation of physiological problems; as in the work done on respiration by the English school of the latter half of the seventeenth century, that school of which we have reason to be proud, which includes Boyle, Hooke, Lower, and Mayow—and as in the researches of Stephen Hales on the physics of the circulation; and thence to be applied to some extent, though as yet to a very limited one, to medical practice. Passing over the intervening period of steady progress in physics and chemistry during the eighteenth century, we come at the end of this century to the celebrated discovery of Galvani (1791). Let us not forget that Galvani as a Professor of Anatomy and Physiology belonged to our profession, for it is hardly too much to say that the splendid achievements of modern electrical science come in no small degree from his first physiological experiments, partly indirectly, indeed, through his controversy with Volta, which led to the discovery by the latter of the voltaic pile and of the production of electric currents by the action of fluids upon metals.[3] From this time onwards the relation between medicine and science undergoes an entire change. The increasing complexity and range of scientific inquiry made it impossible for the worker in science to be at the same time engaged in the practice of physic, and moreover to an ever-increasing extent led him to specialise in one subject. To achieve distinction or to advance knowledge, he began to find that he must limit his work to one branch of science. Hence we no longer find science an avenue to medicine, but that it has become an end in itself; and the names illustrious in science cease, with rare exceptions, to be those of medical men. At the same time medicine itself is about to enter upon a career of rapid and unprecedented development, largely to be attributed to that great growth of scientific knowledge which placed so many new resources at its disposal.

In many branches of medicine science has given us exact knowledge, results which can be weighed and measured, and which can be calculated upon with certainty, as a substitute for empiricism. It has made it possible, although unfortunately to a still too limited extent, to predict that given certain conditions certain results follow. We have seen that as the domain of science extended, greater efficiency necessarily entailed more strict specialisation on the part of the workers, and this same tendency has shown itself as much or more in our own art. The infinitely more extensive, and at the same time more accurate, knowledge in the strict fields of medicine and surgery implies that less time can be devoted by medical men to general scientific studies. In this respect I doubt whether medicine can retain in the future the position that it has held in the past. There can be no doubt that the average level in scientific knowledge of the medical man of the future will be higher than it has ever been before, because of the better training that is given in the sciences that bear directly upon medicine. That contributions to pure science of the same excellence and of the same extent and variety as those made in the past will ever again be produced by medical men is not probable. But, on the other hand, compensation may be found for this loss in the wide and engrossing nature of the problems opened up for investigation in the field of pure medicine, by the application to its theory and practice of the discoveries made in other branches of science. There is no longer need for the doctor to seek outside his own profession for subjects of scientific inquiry ; he can find in his own proper work subjects in which he may confidently expect to advance knowledge, and these neither limited in scope nor tending to narrow his mind, but rather to bring him into close relation with the widest problems of biology. The pursuit of medicine, practised in the right spirit, is one of the few which enables its followers " to see life steadily, and see it whole."

It is the gradual emergence of medicine from the empirical to the scientific stage that has changed so greatly the position of the doctors of the twentieth century as compared to those of former times, and it is from this point of view that we can estimate best the advantages which we possess over our predecessors. I may be pardoned for quoting in this context a well-known passage of Bacon, because it brings out so clearly the change in our profession in these respects. After remarking on one drawback of our calling that " in the opinion of the multitude, witches and old women and impostors have had a competition with physicians," a statement which unfortunately for us, and still more unfortunately for the lay public, is almost as true to-day as in his time, he goes on to say, " Therefore I cannot blame much physicians that they use commonly to intend some other art or practice, which they fancy, more than their profession. For you shall have of them antiquaries, poets, humanists, statesmen, merchants, divines, and in every one of these better seen than in their profession." This passage well exemplifies the change which has come over medicine as a profession, and has raised it again into a calling of wide intellectual interest. It seems to me that it also shows the point of difference between the doctors of our own day and those before the dawn of the modern era. This difference lies in the facts that the advance of medicine as a science, by giving the doctor fresh powers, has also given him confidence in his ability to heal and to increase knowledge, and that it was the absence of this hope of advancing the science and art of his own profession that drove the physician of Bacon's age to seek relief in other pursuits.

Of late years we have heard it said with increasing frequency that the learned physician of cultivated tastes will shortly become extinct. If it is meant by this that physicians will no longer, in Bacon's phrase, be better antiquaries, poets, or humanists than doctors, it is hardly to be regretted. After all, a physician, however eminent he may be in other branches of knowledge, should be learned as a physician first, and erudite in other ways afterwards. But fortunately the very nature of the medical calling brings the doctor into such close touch with all sorts and conditions of men, and with so many different forms of human activity as to ensure that it will always contain men of wide culture. Possibly the physician of the future will attain to culture by ways which diverge from the traditional paths, his erudition may be chiefly in the natural sciences, that is to say in the science and knowledge of his times.

Of the way in which modern science may open out in a totally unforeseen direction a new branch of learning, and with it a new insight into disease and a new hope of progress in the healing art, the study of bacteriology offers a notable example. Passing over the philosophic interest of the discovery of forms of life so infinitesimally small, of a world of minute organisms hitherto undreamt of, the history of bacteriology strikingly illustrates how far-reaching and momentous may be a scientific discovery, which at first sight seems limited in scope. Who could have predicted that the work of Pasteur on ferments would lead to the elucidation of the true nature of infective disease, and (still more remarkable) to the foundation of a new surgery, so extraordinarily successful in its results that it may well claim to be one of the chief scientific triumphs of the end of the nineteenth century. Great as the achievements of modern surgery and the benefits that it has conferred on mankind have been, the advance in the knowledge of infective diseases and of the means by which immunity from them can be secured is no less striking, and promises to be as fruitful in beneficial results. It is difficult to realise that more has been learnt of the nature of infective disease in the last thirty years than during the long ages through which they have been known to mankind; and not only so, but a line of investigation has been started which has by no means come to an end, for before this chapter in the history of medicine is closed we may confidently expect that the mode of exterminating these disorders will have been effectually learnt.

The reproach has been laid against medicine that during the long period between the Hippocratic School and the time of Sydenham it departed from the rule of the former of carefully observing and recording individual cases. Although this will always be a necessary part of medical investigation, and the more fruitful in proportion to the closeness with which clinical observation is kept in touch with the science of the day, yet the advance made in this way is necessarily slow, and the experience of modern times has shown that carefully devised scientific experiments are a necessary adjuvant to it, and lead through wider generalisation to more rapid progress. Further, it has been found that the exhaustive study of special branches of medicine has been rewarded not only by the increased light thrown upon some dark corner of our art, but by fresh additions to the whole realm of medical science.

We have thus briefly retraced the path which medicine has followed in its gradual evolution from empiricism towards the position of an exact science. Can we yet say that it has taken the last and greatest step and attained this position, and, if so, what is its place amongst the exact sciences? The answer to the latter part of this question is fairly obvious, it must be as a branch of biology that medicine takes its place as a science. But instead of the problems dealing with the conditions of survival, increase, and growth with which biology is mainly concerned, medicine is occupied with the departures from the normal physiological standard, with the phenomena of decay or threatened dissolution. Disease not being an entity in itself, we can most usefully conceive of it as a retrogression from the current standard of a healthy living activity. It is as a branch of biology that medicine deals with the results of the constant struggle between man on the one hand and the organisms that war against his existence on the other. So that medicine has to solve and to meet the problems connected with the survival of the dominant race—man—in his struggle with the forces that make for his extinction. We often forget, but should be constantly reminded, that in this internecine struggle nature carefully provides for the survival and growth of the lowest as well as of the highest forms of life. Blind and undiscrimating, she gives an equal chance to all. Hence it has always seemed to me that the "vis medicatrix naturæ," if it is meant by that term, as is so often implied in the common use of it, that nature benevolently works to protect and guard the highest organism—man—is a misnomer. Hence again, though we should all deprecate an unnecessary interference with "natural" processes of recovery from disease, and indeed extended pathological knowledge has both informed us of the course of such processes and warned us of the importance of "non nocere," the doctrine of the "vis medicatrix naturæ" interpreted in the vulgar way leads to a sort of nihilism in medicine, which paralyses further advance in the art of healing. At the most all that the "vis medicatrix" can mean with regard to man and his departures from health is that in the course of ages his organs and tissues have attained to a position of equilibrium in working which is consonant with his best activity, and that when this equilibrium is disturbed by the incidence of disease there is in the majority of cases a tendency for it to be re-established.

Returning now to inquire into the conditions which must be fulfilled to constitute medicine an exact science, we find that, roughly stated, they are the following: (1) The causes of disease must be known; (2) the precise alterations produced in the anatomical and chemical constitution of the body, and the exact organs and tissues affected must be ascertained; (3) the course which a disease runs and the results, if it is one which causes as sequelæ, temporary or permanent changes in organs and tissues, and in their secretions, must be determined; and (4) we should be able, given the conditions, to reproduce the disease at will. It is enough to constitute medicine as an exact science if we can satisfy these conditions for some diseases only. If in other words there is a sufficient knowledge of the general laws which control, and of the phenomena which characterise, certain diseases, to enable us to lay down general principles on which those still imperfectly known can be worked out in a scientific manner.

The history of medicine in recent years gives many striking instances in which diseases imperfectly known or even new to us have been investigated with complete success by the application of methods founded on general principles established by observation and experiment in similar affections. What better examples could be taken than the recent discoveries in malaria and in the less known tropical diseases, such as the disorders caused by trypanosomes.

With regard to the exhaustive investigation of a disease in the ways indicated above, this has of late years been accomplished in many instances. Turning to the infective disorders, and taking for instance anthrax or tetanus, we know the cause, the nature of the poisons at work, the anatomico-pathological changes produced in the organs, the course of the disease, and, in the case of tetanus, the mode and exact seat of the peculiar combination of the toxin with the cytoplasm of certain highly-specialised cells. We can reproduce the disease, and not only produce it, but so regulate the dose of the poison as to give a mild or severe attack; and, lastly, we can confer immunity against an attack by methods the principle of whose action is understood. In these infective disorders then, which form so large and important a branch of medicine, the advances in knowledge which have been made are so great as to constitute alone a well-founded claim for medicine as an exact science.

Perhaps, in nervous diseases, our acquaintance with the seat and nature of the anatomico-pathological lesions and with the finer changes in the protoplasm of cells is more complete than in any others. This knowledge has been acquired by utilising the extreme degree to which differentiation of function has been carried in the gradual evolution of the nervous system. The progress that has been made in the knowledge of the structure and function of this part of the body during the last generation is remarkable. But though the mode of action of certain poisons and toxins has been ascertained and the selective affinity of some of them for definite tracts and centres has thrown much light on the action of poisons in general, we are very much behindhand in our knowledge of the exact causes of nervous diseases If we could make one step forward, and recent work has given us fresh hope of this, we should fill a most important gap in scientific medicine—I mean if the organism of syphilis were discovered and its life-history known. If in this one disease we could work out the life-history of the organism and ascertain its chemical products, we should, by combining these fresh acquisitions with the already acquired accurate knowledge of the anatomical lesions, not only obtain a complete picture of the course of a most important disease, but incidentally get fresh light on the conditions underlying other nervous affections. It seems to me that we are close to the time when our knowledge of nervous disease will give medicine another title to be an exact science.

To take another example, and this time from the chemical side of medical work. No better example of the replacing of empiricism by scientific experiment could be given than is afforded by modern pharmacology in its investigation of the relation between chemical constitution and physiological action, and of the physiological effects of introducing various chemical groups into complex organic compounds whose physiological action is known. Then the recent experiments on digestion have taught us that cells, differing little in morphological characters, may show an unexpected differentiation of function. Recognition of functional differentiation of this kind is of the very essence of exactness in clinical work, and these experiments afford good evidence that parts of organs hitherto regarded as practically identical may in reality carry on distinct and highly specialised activities.

In spite of these many and great advances, we have, however, still to deal in too large a field of disease with the uncertainty of result, which from a scientific standpoint is the bane of clinical medicine. Hence, to quote again from the passage of Bacon which I cited above, it is still true of our position as medical men " that the physician . . . hath no particular acts demonstrative of his ability, but is judged most by the event; which is ever but as it is taken: for who can tell if a patient die or recover, . . . whether it be art or accident. And therefore many times the impostor is prized, and the man of virtue taxed."

Many factors contribute to this uncertainty of result in actual practice. One of them is to be assigned to what is commonly known as the "idiosyncrasy" of the patient, but may be better termed the variable reaction of the individual, an unknown quantity for which large allowance has to be made in practice, and which often comes to baffle the best directed efforts at treatment and the most carefully-considered prognostications. Possibly to some minds, with a natural bent for speculation and theoretic inquiry, the very uncertainty of the issue in the individual possesses a charm in itself, as a food for thought and philosophic questioning. But however fascinating in the theory of medicine the problem of individual variation may be, it is anything but pleasing in the daily practice of our profession. We must long for the time when we shall be able to do our clinical work with exactness, and to look with confidence for precision of result. Another and still more potent cause of failure of our best directed efforts lies in the extreme complexity of the problems often presented in clinical medicine. There are causes at work which we fail to recognise, or we are misled by certain symptoms to attach undue importance to some minor factor, and to overlook the true cause of disease, either because at the time of investigation it may not be giving rise to clear signs, or, although present, their significance is not appreciated. The variation of the pathological processes that take place during the course of a long and complicated disease is also difficult to estimate aright. It results that when the work has been done in the most accurate and careful way possible we are confronted with a mortifying failure because the value of a certain factor or factors has not been correctly calculated. Such are two of the most obvious conditions which have in all times, and do now, render the practice of clinical medicine unsatisfactory from the standpoint of the scientific worker and expose the practitioner to unmerited reproach.

The remedy is to be sought in the increasing application of scientific methods to medicine, and it is to modern science that we must look to remove such obstacles from the path of medical progress. After all, when we speak of idiosyncrasy as altering the ordinary course of a disease we are but exposing our own ignorance. Diseases, like all other natural phenomena, move by exact laws, and the individual variations which now baffle us would appear, if our views were wide enough and our knowledge deeper, but as expressions of the action of these general laws.

In closing this inadequate summary of the relation between medicine and science, I may allude to one danger which it seems to me may impede our future advance, and that arises from the increasing specialisation which appears to be the necessary correlative of latter-day progress in all branches of science. The day of the encyclopædist in science seems to have passed. It is impossible for even a Darwin or a Kelvin to be in the first rank in more than one or two branches of it. This development of specialisation may lead to such an increase of technicality in methods of work and in the terms in which they are described as to make it barely possible for the workers in one branch of science to thoroughly appreciate what is being done by those engaged in another, so as to be capable of turning recent discoveries to account in their own special province.

From this cause there is a danger that medicine should again become too stereotyped, and thereby lose that close connection and interdependence with other sciences which have been so laboriously built up during the past three hundred years, and from which it has derived such enormous advantage. Should this unfortunately occur, it seems to me that, in spite of all the great advances that have been made, there might again ensue one of those sterile periods in our art in which once more "systems," with their arid and barren theories, would take the place of that constant scientific observation which is essential to true progress. It may seem impossible now that we have gone so far that our practice should become retrocedent, but it must be remembered that in former times men have been equally well satisfied with the extent of their knowledge. For instance, in the Roman civilisation of the age of the Antonines, which offers so many striking resemblances to our own era, a very high degree of material prosperity was reached. Men talked just as readily as we do now of the resources of modern civilisation, and probably the troups of students who followed Galen from bedside to bedside of his patients would have scouted the idea that their knowledge of medicine left much to be desired.

The remedy lies in constant and strenuous exertion to keep the science and art of medicine in close touch—no easy task—with every advance in biology, chemistry, and physics, that as science continually extends her beneficent domain, and as "the old order changeth, yielding place to new," medicine may, by taking and holding fast what is of permanent good in both new and old, fight with ever-increasing success against disease and death.

## REFERENCES.

[1] I use the term medicine in its wider and proper sense to comprise both medicine, surgery, and all their branches.

[2] Michael Foster, *Lectures on the History of Physiology*, Camb. Univ. Press, 1901.

[3] McKendrick, *Life in Motion*, 1902.

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# CASES ILLUSTRATING THE MORE UNUSUAL COMPLICATIONS OF PNEUMONIA.

THE following cases illustrate some of the rarer complications met with in pneumonia. The occurrence of such complications forms one of the strongest arguments in support of the modern conception of pneumonia as a general infection. These instances occurred in a consecutive series of 126 cases of pneumonia. They comprise PERITONITIS (2); THROMBOSIS OF VESSELS (3), in one of which there was also general pneumococcic infection; ENDOCARDITIS (2); NEPHRITIS (1); ARTHRITIS (1). In the same series there were also three cases of delayed or imperfect resolution of the consolidated lung, and three cases of empyema, neither of which I have thought it worth while to report. With regard to cases of imperfect or absent resolution, it may be remarked, however, that if an example of this condition comes under observation for the first time at some considerable interval after the original illness, valuable aid is given in diagnosis by the common circumstance that the consolidated area corresponds exactly to the superficial delimitation of one lobe of a lung on the surface of the chest.

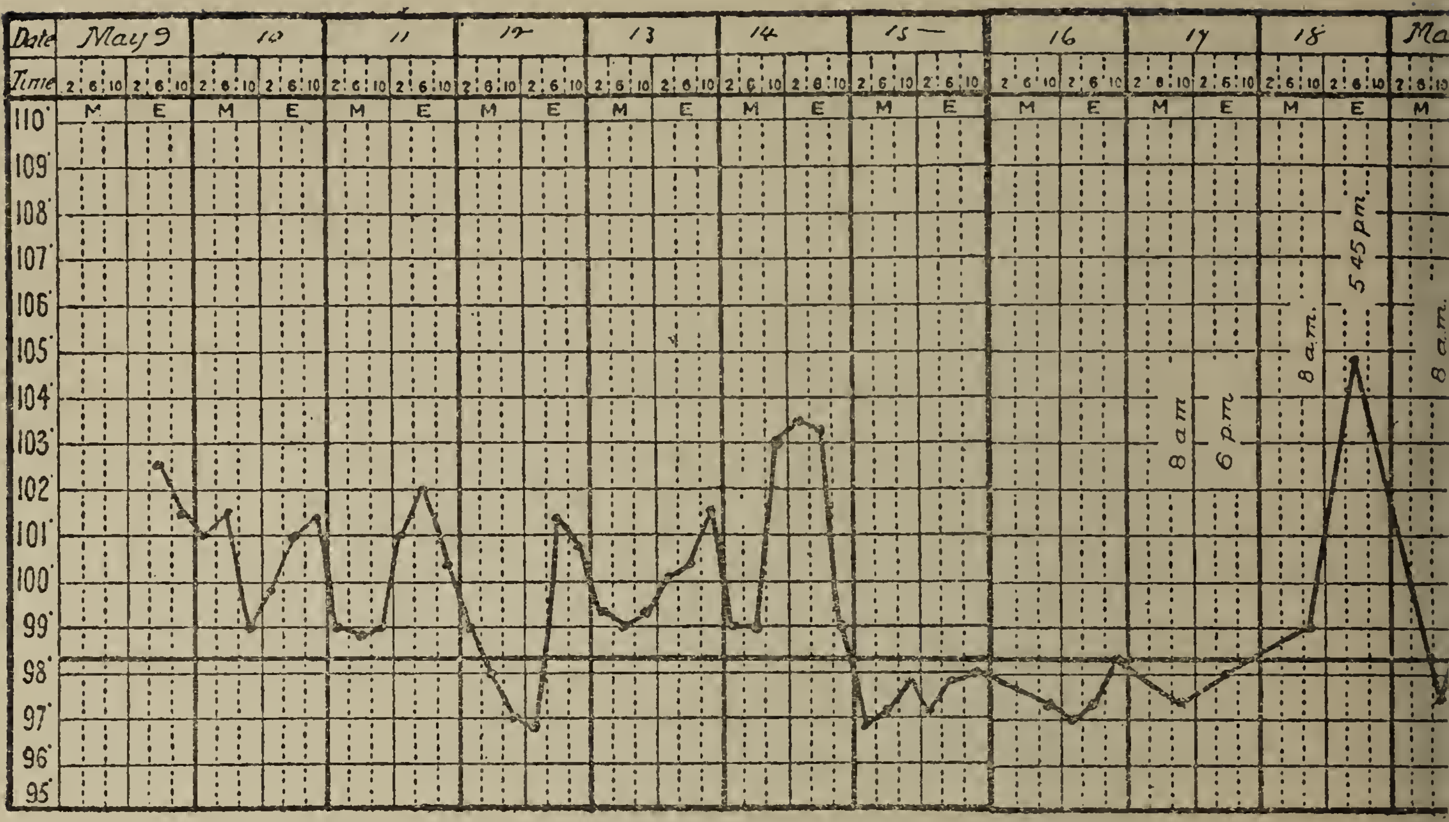
There is also a point of importance in empyemata following pneumonia, that is, that at an early stage firm adhesions may unite the visceral and parietal pleuræ along the septa between the lobes of the lung, and thus on the right side there may be a collection of pus over the lower lobe entirely shut off by adhesions along the interlobar septum from another smaller collection over the middle lobe. This happened in one of the above cases of empyema, in which after the pus had been evacuated from an empyema over the right lower lobe it was found necessary to do a further operation for a small collection of pus exactly corresponding to the superficial extent of the middle lobe, and completely shut off from the first one.

Pneumococcic Peritonitis.—Peritonitis is a rare complication of pneumonia, although, as is well known, severe pain in the upper part of the abdomen accompanied by great diminution in the respiratory movements in the same situation is common, and occasionally leads to errors in diagnosis. Though peritonitis is said to occur in pneumonia by direct extension through the diaphragm, it would seem more generally the result of a general pneumococcic infection, as appears likely in the following instances, which occurred in two sisters.

Winifred B., æt. 9, admitted February 7th. The patient when æt. 3 had several attacks of convulsions, but with this exception, although never robust, she had had no serious illness. On January 15th she went to school apparently in good health, but returned midday with a pain in her stomach, and vomited. The next day she was delirious, but this delirium soon passed off. During the next fortnight she suffered from severe paroxysmal pain in the abdomen, relieved by rubbing it. For the first week she was repeatedly sick, and the abdomen swelled and became hard. She had a troublesome, painful cough, the tongue was thickly furred, and an eruption of labial herpes appeared.

On February 1st the skin gave way over the umbilicus, and about two quarts of thin, greenish-yellow fluid were discharged, with great relief to the pain. Since that day there had been a slight discharge from the umbilicus. The bowels were moved regularly throughout. On admission the child was thin and emaciated, with the remains of labial herpes about the mouth.

On admission, February 7th, the chest was small and badly formed. There was some dulness over the base of the right lung, with coarse râles in the axillary region, and over the left base bronchial breathing and some small crepitations. The heart was normal. The abdomen was distended, its walls rigid, and there was a feeling of resistance about the abdomen generally. It moved on respiration. There was a sinus, discharging pus, at the umbilicus. There was dulness over the front of the abdomen,



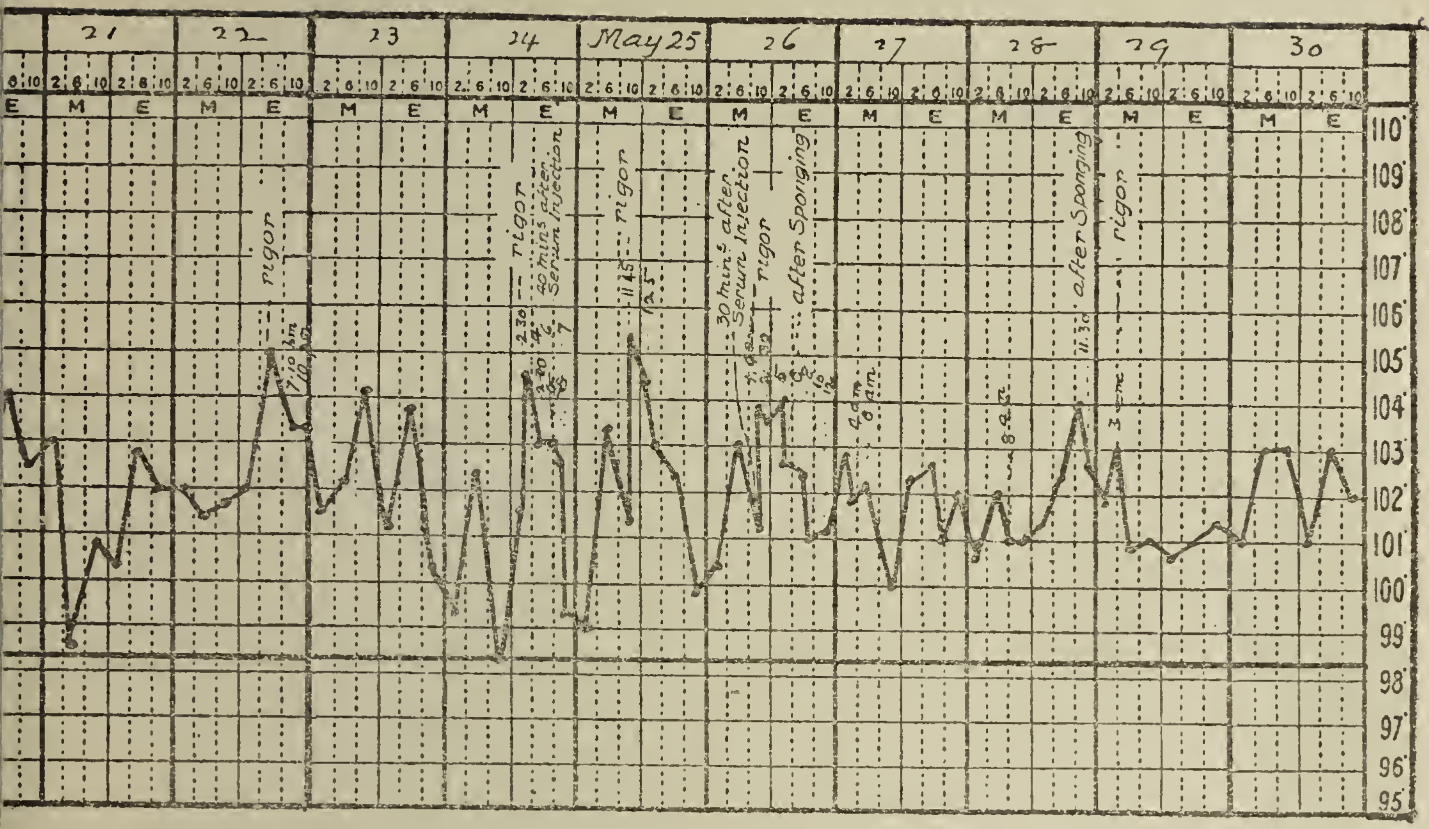
*Temperature Chart. General Pneu*

but the flanks were resonant and there was no evidence of free fluid. The temperature was hectic, varying between normal in the morning and 101° at night.

The general appearance of the child and the physical signs in the abdomen suggested abdominal tuberculosis ; examination of the pus from the sinus, however, showed no tubercle bacilli, but the pneumococcus was obtained in pure culture.

The blood gave erythrocytes 2,650,000, white corpuscles 15,000 to c.mm. A small incision was made just below the umbilicus, and a large cavity, shut off from the rest of the peritoneum was discovered between the omentum and the anterior abdominal wall, from which about two pints of pus was evacuated. After the operation the temperature fell to normal, the sinus gradually closed up, and she left the hospital quite well five weeks later.

On March 2nd Bessie B., æt. 4, the sister of the above patient, was admitted, with the history that on January 24th, three days after her sister was taken ill, she developed a bad cold, with fits of shivering and several attacks of vomiting. During the next two weeks she was very ill with high fever, a bad cough, and pains in the chest and abdomen. The pains in the abdomen were paroxysmal, at times very severe, and were relieved by poultices. There was diarrhœa at first, but the bowels were afterwards moved regularly. The vomiting ceased after the first week. The abdomen became swollen, distended, and hard,



*Infection. Thrombosis of Vessels.*

and as the child did not get better, she was brought to the hospital.

On admission the child was pale and emaciated. There were a few scattered râles at the bases of the lungs, otherwise there were no abnormal physical signs in the chest. The pulse was 120; respiration 30; temperature 99.5°. The abdomen was much distended, measuring 22½ inches at umbilicus. It was dull all over, except in the epigastric region. There was a distinct fluid thrill. The skin around the umbilicus was red and dusky. The abdomen moved very little with respiration.

The day after admission Mr. Morton made a small incision between the umbilicus and xiphoid cartilage, and evacuated a large quantity of greenish yellow, fairly thick pus. On examination the organisms obtained gave the cultural characteristics of the pneumococcus. The after history of the case was uneventful, the discharge rapidly diminished, and the patient left the hospital quite well twenty-five days later.

The interesting point is the occurrence of the same complication, and that an uncommon one, in two sisters, and also, in the first case, the close resemblance clinically to abdominal tuberculosis. The diagnosis was cleared up by the discovery of the pneumococcus in the pus.

Cases of Thrombosis of Vessels.—Thrombosis is a rare complication of pneumonia. In 27 out of 32 cases collected by Steiner the time of its appearance was during convalescence. According to Osler, it nearly always occurs in the femoral veins, and is still more uncommon in arteries than in veins.

*Thrombosis of Left Superficial Femoral Vein.*—The patient was a strong, healthy collier, of temperate habits. He had a severe chill on December 24th, and on the 25th a rigor with pain in the left side of the chest, and was admitted into hospital on 26th with the signs of lobar pneumonia at the left base. The course of the pneumonia was uneventful, and terminated by crisis on December 31st. The heart's action was well sustained throughout; there were no murmurs; the pulse was good, varying from 80—96. A leucocyte count on the fifth day gave 45,000 to c.mm. The urine was normal. On the thirteenth day, when convalescence was apparently proceeding normally, the temperature, which had been normal for five days, rose to 99.5°, and he complained of pain in the left groin and calf, and the left thigh and leg swelled with great rapidity. The next day a hard, tender, band-like swelling could be felt along the course of the left superficial femoral vein, and there was a swollen vein on the calf leading up to this. There was no further constitutional disturbance, and no sign of any heart affection. Under the usual treatment pain and swelling gradually subsided, and by the end of January all evidence of the thrombosis had disappeared. He left the hospital well on February 3rd.

The most notable feature of the case is the rapid onset, and the equally rapid clearing up of the lesion, in marked contrast with the tedious course of most cases of thrombosis of the femoral vein. The cause was obscure; there was no general infection, and no affection of the heart, whilst the well-marked leucocytosis in a moderately severe attack of pneumonia showed that the patient's resistance was good.

*Thrombosis of Cerebral Vessels.*—J. H., æt. 25, had always enjoyed good health, but was said to have had a slight discharge from the right ear before present attack. It was doubtful, however, whether this discharge was more than a little wax. He had felt ill for a week before, being obliged to give up work on October 28th. He was first seen by Mr. E. H. C. Pauli on October 31st, who found that his temperature was 102°, and that there was pneumonia of the lower lobe of the right lung. The crisis occurred on November 1st, and he was apparently doing well, when on November 3rd he had two slight rigors, an attack of general epileptiform convulsions, and his temperature, previously normal, rose to 101°. He vomited several times, and complained of headache. The temperature remained at about 102°; there was no paralysis of any muscles, no recurrence of rigors, nor fresh symptoms, but on November 4th he became drowsy, and this gradually deepened into coma.

On November 6th, when I saw him, he was in a condition of moderately deep coma: he did not speak, but opened his eyes when shouted at. The pulse was 120; the respiration 32, irregular and often sighing. There was deficient resonance over the base of the right lung, and *redux* crepitant râles were heard here. The cardiac apex beat and area of dulness were normal, the pulmonary second sound accentuated and the first sound at the apex indistinct. Abdominal organs normal. The pupils acted to light, and were of moderate size, the right larger than the left. There was no localised paralysis; he could move his limbs; the arms were flaccid, the legs a little rigid at the knees. There was no rigidity of the neck muscles. The knee-jerks were present, not increased; the plantar reflexes were extensor in character; there was no ankle-clonus.

He could not swallow on this day; and there had been incontinence of urine and fæces for two days. The right ear contained wax, so that the drum could not be seen. The outline of the optic discs appeared a little blurred, but they were not hyperæmic, and there was no definite optic neuritis. On making a lumbar puncture, about 1½ ounces of perfectly clear, limpid fluid without any deposit were withdrawn.

In view of the difficulty of diagnosis in this case, the result of the lumbar puncture was especially important, as it enabled one to exclude meningitis, and probably intra-cranial abscess, a possible complication in view of the uncertain history of discharge from the ear. Thrombosis of cerebral veins was thought to be the most probable diagnosis.

The patient died the same evening. An examination of the brain was made at his home under considerable difficulties. Unfortunately, the result of this examination was negative, as the exact cause of the cerebral symptoms was not made out, but it was valuable as proving the absence of meningitis and intra-cranial abscess. Thrombosis of cerebral vessels is not always easily recognised, especially under the conditions in which the examination of the brain was made in this case; and I think that this was the probable cause of death.

Apart from meningitis, paralysis of cerebral origin, generally hemiplegic, but sometimes monoplegic, occasionally occurs in pneumonia, either early in the disease or during convalescence.

In some of these cases of hemiplegia no gross lesion is found after death, and they are often attributed to the effects of toxins.

In those cases in which there is a *post-mortem* lesion, it is generally softening from embolism or thrombosis. Probably in some cases reported as without lesion a patch of recent softening has escaped notice, which, if it is small, is quite possible.

*General Pneumococcic Infection—Thrombosis of Vessels.*—The patient, E. C., was a horse-driver, æt. 23, who had never had a day's illness previously. The illness began with pains in the head on May 5th, followed on 6th by purulent discharge from the left ear, and on the 7th by severe pain in the left side of the chest, which interfered with respiration, and by vomiting. He was admitted to hospital on May 8th with well-marked signs of pneumonia of the lower lobe of the left lung. The heart was normal, the area of dulness not increased, and the pulmonary second sound well accentuated. Pulse 80; respiration rate 60; temperature 102.5°; leucocytes 18,750 to c.mm. Urine contained no sugar or albumin. Chlorides greatly deficient. He went on fairly well until the eighth day, when he had a rigor, and his temperature rose to 105°. It was noticed that his neck was swollen, and that there was thrombosis of the left median basilic vein extending into the basilic and median cephalic veins, the left forearm being swollen. The leucocyte count was now 25,700 to c.mm.; erythrocytes 4,000,000; hæmoglobin 90 per cent.

The following three days the temperature was normal, and the patient felt much better. On the twelfth day the temperature suddenly rose again to 105°. On this day a culture made from blood taken from the right arm showed a pure growth of pneumococci. During the next few days the patient felt better, in spite of the high range of temperature. Further, his tongue was red and dry, and his pulse, which had previously been about 68—72, now varied from 116—124. Leucocytes 21,800 to c.mm. The physical signs at the left base indicated that the consolidation was slowly clearing up in spite of the grave constitutional symptoms.

On the twenty-second day of the illness 5 cc. of antipneumococcic serum were injected. On the previous day he had had another rigor, and rise of temperature to 105°. The leucocyte count was now 19,375 to c.mm. A trace of albumin had appeared in the urine, which also gave a distinct band of urobilin.

On the twenty-fourth day, as the fever still continued high. and the rigors recurred daily, a second injection of 5 cc. serum was given, with no appreciable effect, unless a fall of temperature from 103° to 101° was so reckoned.

There had been no extension of the thrombosis in the veins of the left arm, which remained limited to the veins in which it first appeared. No other thrombosed veins were detected elsewhere. There was no enlargement of the spleen that could be detected clinically at any period of the illness. The physical signs in the lungs remained stationary, the consolidation only partly clearing up.

On the twenty-eighth day of the disease the temperature was lower, at about 102°, but he was wandering in mind, looked haggard and emaciated, was sweating profusely, had partial incontinence of urine, and was obviously sinking. He died two days later.

The result of the *post-mortem* examination confirmed the diagnosis made during life. The thrombosis here was undoubtedly part of a severe general pneumococcic infection, and the gravity of the case was due to this latter condition, and not to the thrombosis, which could only be considered an incident in the illness, and not contributing to the lethal result.

ENDOCARDITIS.—*Double Pneumonia.*—Maurice Y., æt. 19, engine cleaner. There was no history of any previous illness. For a few weeks the patient had suffered from an obstinate cold in the head, when on October 5th he was taken with pain in the right side of the chest, cough, fever and profuse sweats. He went to bed, and the next day the symptoms had increased, and he coughed up some rusty, tenacious sputum.

He was admitted on October 9th with well-marked signs of consolidation of the lower lobe of the right lung, and there was also dulness and bronchial breathing at the left base. The heart's apex was in the normal position, and the area of cardiac dulness normal. No murmur was heard. The temperature was 103°; pulse 90; respiration 30, shallow and irregular.

On October 10th the signs at the left base had increased, and now indicated extensive consolidation of the lower lobe of the left lung. A pleuritic rub was audible all over this lobe, and there was also well-marked pleuro-pericardial friction. The temperature was 102° on this and the following day, October 11th, when his pulse was 130, respiration 50. No cardiac murmur could be heard, possibly on account of the loud friction sounds which were present throughout. On this day he became suddenly worse after a violent fit of coughing, was deeply cyanosed, and died of heart failure.

*Post-mortem.*—There was extensive acute pleurisy over the whole of both lungs. Nearly the whole of the right lung was in a state of red, passing in places into grey, consolidation, and the lower lobe of the left showed red hepatisation. The heart cavities were dilated, especially on the right side. On the mitral valves were some old granulations, and in addition on these and on the edge of the valve segments were numerous recent small granulations. Scrapings of the cut surface of the consolidated lung showed numbers of pneumococci, which were also obtained from the recent granulations on the mitral valve. The other cardiac valves were healthy.

Endocarditis is not a common complication of pneumonia. In the form of which the preceding case is an example it often goes unrecognised. In this case there was no evidence from the previous history or symptoms of the old existing lesion of mitral valve, and, further, there were no signs of the acute endocarditis supervening on this old lesion of the valve during the fatal illness. Any mitral murmur during this illness would have been effectually concealed by the loud friction sounds. The low temperature throughout such a severe attack of pneumonia is an unfavourable symptom, indicating poor powers of resistance on the part of the patient. Endocarditis in pneumonia generally affects the left side of the heart, and the pneumococcus is usually the active agent. As to its frequency, Preble, from an exhaustive analysis of over 20,000 cases, gives it as 1 per cent. of all and 5 per cent. of fatal cases. Pneumococcic endocarditis is frequently accompanied by meningitis, so that cerebral symptoms may form the predominant feature of the illness. Both this and the following case illustrate the well-established fact that cardiac valves which are the seat of previous disease are especially liable to be attacked by the micro-organisms of any subsequent acute infection.

*Pneumococcic* (*Ulcerative*) *Endocarditis.*—Charles M., æt. 47, a clerk, had scarlet fever as a child, and at the age of 22 was told by a medical man that he had heart disease. Except for occasional attacks of palpitation he remained well, and was able to do his work until April, 1900, when he was laid up with fever, cough, and pain in the right side, and was treated for a "liver attack." After this he got about again, but felt weak, and six weeks before admission took to bed on account of increasing weakness. He had a rise of temperature every evening, with profuse sweats between 3 and 6 a.m. There were no other symptoms, except a slight attack of hæmaturia three weeks before admission, and a rash consisting of bright red spots over the legs.

On admission he looked ill, and was anæmic and sallow. The temperature was 102° ; the pulse 96, collapsing ; respiration 26. There was a fading purpuric rash on the legs.

On examination the breath sounds were harsh, the lungs otherwise normal. The heart was much enlarged, the apex beat being two inches outside the left nipple. There was a marked diastolic thrill at the apex, and a loud systolic murmur there. At the base there was also a rough systolic murmur, followed by a long soft diastolic murmur conducted down the sternum. All the visible arteries showed marked pulsation, and capillary pulsation was also observed. The urine contained a little blood and albumin. The liver was slightly enlarged. The spleen was distinctly enlarged, its tip being felt about two inches below the lower border of the ribs. There were no retinal hæmorrhages, and the optic discs were normal.

The temperature chart shows the irregular course of the fever, and the high range to which it reached. There were profuse nocturnal sweats. The symptoms and physical signs made the diagnosis of malignant endocarditis obvious. Blood was withdrawn from the veins of the arm on three occasions, in order if possible to ascertain the cause of the infection, but no micro-organisms could be recovered from it. At this time the history of the beginning of the illness, when he was treated for "liver complaint," did not have the significance which it afterwards obtained in the light of the pathological findings. In the absence of evidence of the organism present, it was thought advisable to try anti-streptococcic serum. Three brands of serum were employed, one of them being a polyvalent anti-streptococcic serum, and were given in doses of from 10—30 cc. In all 480 cc. were injected, so that a thorough trial of the serum was made. Neither of them had any appreciable effect either for bad or good, except for occasional local redness, infiltration, and tenderness at the site of injection.

He grew steadily worse, and on October 15th slight general anasarca and ascites appeared. This gradually increased, and œdema of the ankles was marked on October 22nd.

On October 26th there was thrombosis of the superficial veins of the right calf, and a fresh petechial eruption appeared over the left thigh and knee. The albumin in the urine increased. About this date he became much weaker and delirious at night. The heart's action became weaker and very irregular. The murmurs persisted as at first.

On October 30th there were signs of a little fluid in the pleural cavities and congestion of the bases of the lungs. He died on November 4th.

*Post-mortem.*—There was a large infarct into the upper lobe of right lung. The lower lobe of the left lung was completely airless, dark red, solid, and granular on section. The heart was greatly enlarged; both ventricles much dilated. On the auricular surface and free borders of the tricuspid valve segments were large masses of fungating, soft granulations, which extended on to the chordæ tendineæ. The mitral valves were much thickened and contracted, but contained no granulations. The pulmonary valves were normal. Aortic valves were largely destroyed, one segment almost entirely, and covered by large masses of granulation tissue. Scrapings from the valves, from the spleen, and from the pulmonary lesions showed abundant pneumococci, which were also stained in situ in sections made of the granulation tissue on the cardiac valves. The kidneys showed subacute nephritis, and there were a few small hæmorrhagic infarcts in the jejunum.

There was no ground for the employment of anti-streptococcic serum in this case beyond the fact that a streptococcus is the most common cause of malignant endocarditis, and in the failure of all attempts to determine the exact organism present, and in view of the grave character of the illness, it was thought right to act on the hypothesis that this organism might be present. It shows, however, the fallacy of employing any serum in the absence of exact evidence of the kind of organism causing an infective illness. Looking back in the light of the *post-mortem*, the "liver attack" of the preceding April was probably a mild attack of pneumonia, but the history was too inconclusive for us to be able to come to any conclusion during life.

NEPHRITIS.—E. P., æt. 10. The patient's mother was taken ill with pneumonia on May 13th, and her father on June 2nd. The patient's illness began on June 6th with pain in the side, cough, fever, sickness, and diarrhœa. She did not sleep in the same room with her parents. She was admitted to the hospital on June 13th. She had not passed any urine for forty-eight hours before admission, and what was passed just before this period of suppression was the colour of blood. She was delirious at night.

On admission the temperature was 103°, pulse rate 104, respiration 42. The tongue was thickly furred. On examining the chest, there was pneumonic consolidation of the lower lobe of the right lung. The heart's apex beat was in the fourth space, and the cardiac dulness extended half an inch over the right border of the sternum. There were no murmurs. There was no enlargement of either liver or spleen. A leucocyte count gave 28,900 to c.mm. A few ounces of urine were passed.

which contained a large quantity of albumin, much blood, and blood and epithelial casts.

On June 15th—16th (ninth and tenth days of disease) she was delirious, with a temperature rising to 104°, pulse 112, respiration 44. The abdomen was swollen and tense ; the urine showed the same characters as above. Pallor of face and puffiness of lower eyelids were marked.

On the eleventh and twelfth days of the illness the crisis occurred, and on the following days the affected lung showed signs of resolution. Respiration fell to 24, and pulse to 72.

On June 20th (fourteenth day of illness) urine contained blood ; epithelial, blood and leucocyte casts, with crystals of uric acid ; there was still a large amount of albumin. Quantity passed, 32 ounces ; urea in 24 hours, 26.5 grms. A leucocyte count on this day gave 28,000 to c.mm., and on June 26th 20,400 per c.mm.

Between June 20th and 26th the daily quantity of urine was only 16 to 20 ounces ; on the latter date its sp. gr. was 1020, with no blood, no casts, and only a small quantity of albumin. The lung continued to undergo normal resolution, and by July 9th the mischief there had cleared up. On this day examination of the urine gave : quantity 24 ounces ; sp. gr. 1020 ; urea daily excretion about 15 grms. on a milk diet with one egg ; a trace of albumin only ; uric acid and calcium oxalate crystals, epithelial cells from urinary passages, and a few granular casts.

On July 17th and 24th the face was puffy, and there was still a trace of albumin in the urine ; otherwise the child seemed well. At the end of this month the urine was passed in normal amount with a sp. gr. of 1020 ; it contained no albumin and no deposit, and she was discharged well on August 5th.

No pneumococci were found at any time in the urinary deposit. Nephritis is a very rare consequence of pneumonia. This is the only case I have ever seen. I think there can be no doubt of cause and effect in this case. In so completely and quickly clearing up, it followed the usual course of nephritis in acute infective disease. The case is a good instance of *infective* pneumonia, and in the infective form the disease is well known to be more severe, more apt to be a general infection, and therefore to lead to complications.

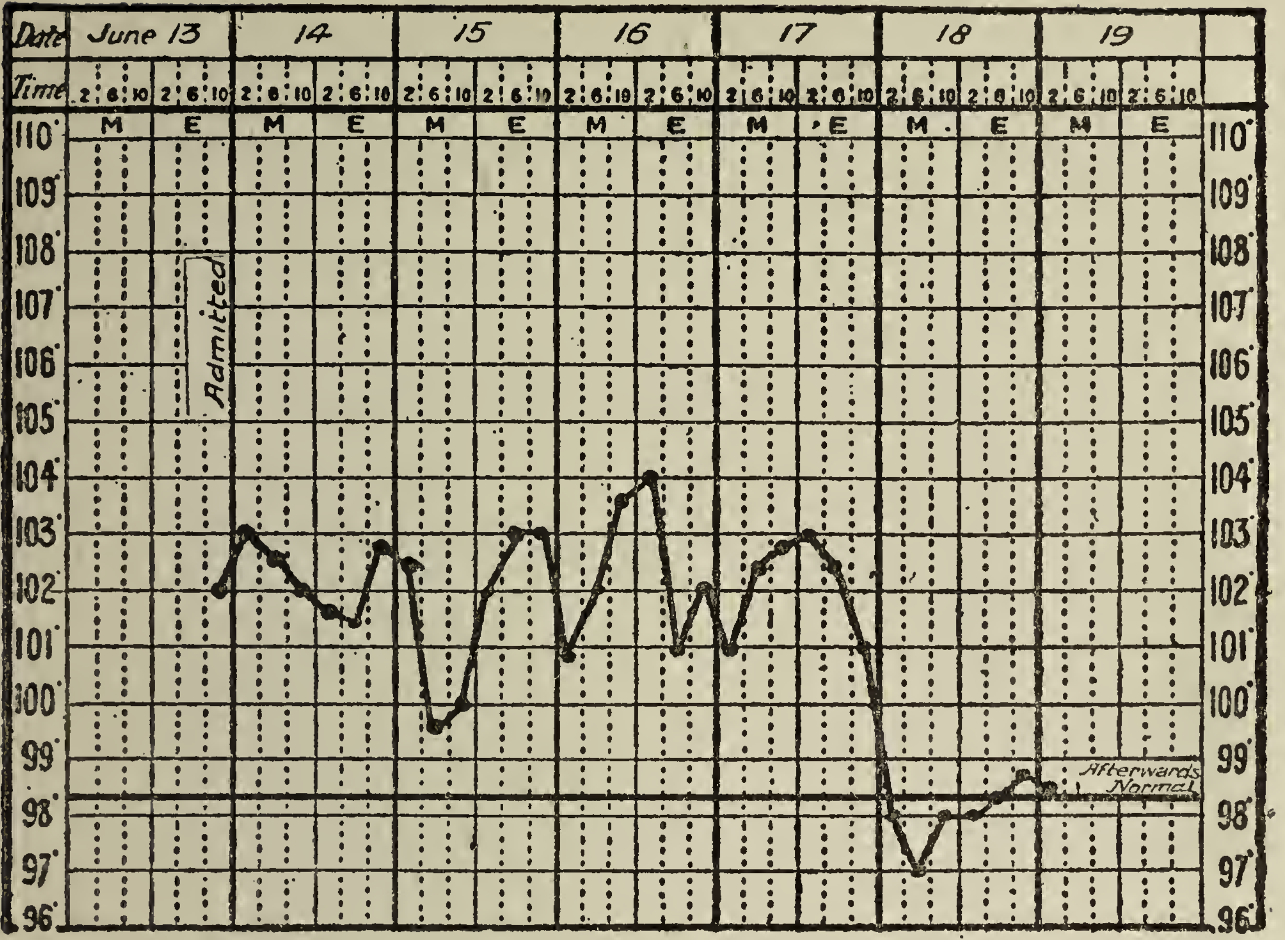
Pneumonia, Empyema, Arthritis.—Victor R., æt. 8, previously healthy. On April 16th, 1906, patient fell into a pool of water ; on the 17th pains in the right hypochondrium and side of chest, followed on 18th by cough and pains in the left arm.

On 21st he was admitted into the hospital with a temperature of 102°, pulse 120, respiration 34. On examining the chest there was dulness, deficient air entry, a few moist crepitations, and increased vocal resonance over the base of the right lung. The other organs were normal. The left elbow-joint was swollen, red, and painful, and there was some fluctuation in the joint. On April 23rd there was a patch of bronchial breathing at the lower angle of the right scapula, otherwise the lung signs remained the same. The swelling of the elbow-joint also remained stationary ; the pain was relieved by placing it upon a splint. The signs of an empyema having developed, on May 4th a portion of the eighth rib was excised, and a moderate quantity of thick yellow pus evacuated. The pus contained numbers of pneumococci. At the same time two incisions were made into the elbow-joint, but no pus found. On May 14th there was no pain in the elbow, and the swelling had much diminished, but the joint was stiff, with very little movement of flexion or extension, the former not beyond a right angle.

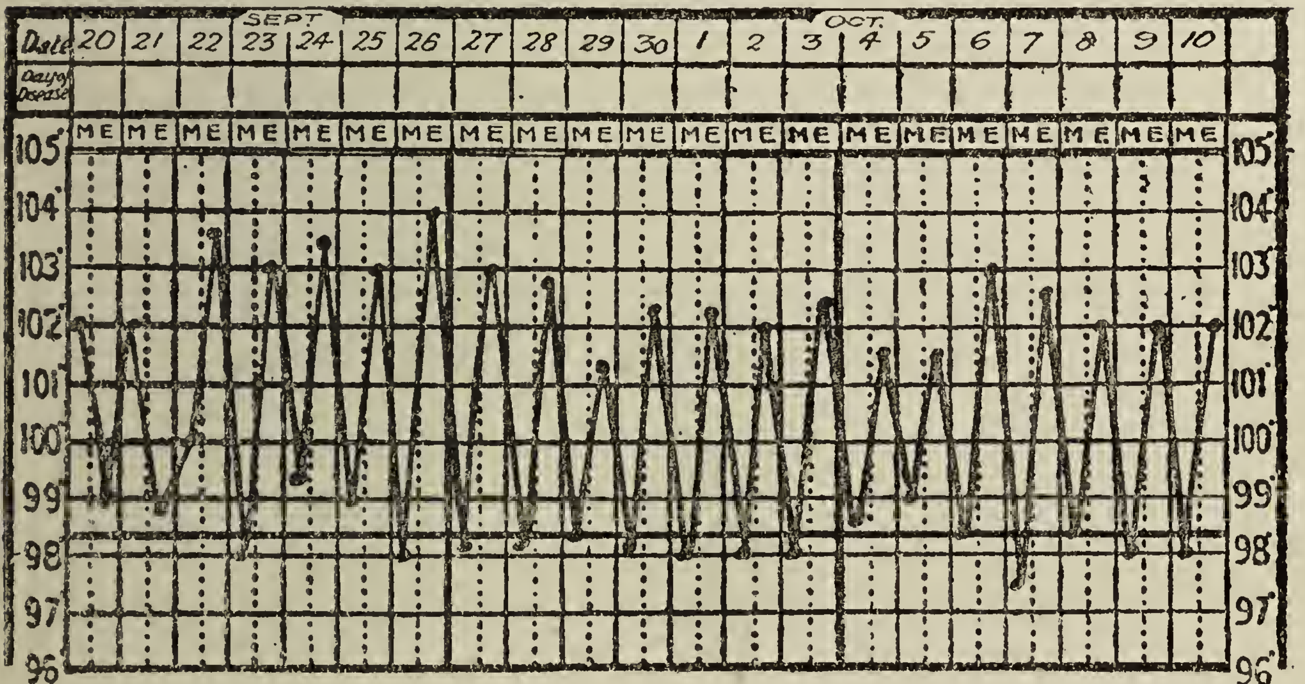
On May 17th the condition of the left elbow-joint still suggested the presence of pus, but none was found. The muscles of the arm were now much wasted, more especially the triceps. On the next day massage of the limb and gentle passive movements of the joint were begun. A curious feature of the case was the appearance of four or five large pustules on the left ankle and foot, which gradually died away, to be succeeded by a fresh crop on June 8th, which lasted until June 20th.

Another feature was that, although the empyema was opened and drained freely, and did well, the discharge gradually lessening, and there being no evidence whatever of retained pus, the temperature remained of a hectic type, ranging between 99° and 102°, for a fortnight after the operation before it returned to normal.

For the rest it is sufficient to say that the empyema wound healed about the middle of June, leaving a very good result as regards expansion of the lung, and that the swelling and stiffness of the joint gradually improved, so that when he left the hospital in July all movements were perfect and the joint appeared normal.



*Case of Pneumococcic Nephritis.*



*To show range of temperature in case of Pneumococcic (Malignant) Endocarditis.*

# A CASE OF ACUTE LYMPHADENOMA.

The following case seems worthy of record, because it affords an opportunity of studying the pathological changes in lymphadenoma running an acute course, a rare occurrence. The clinical features were, in brief, as follows :—

The patient, a youth, æt. 18, had never had syphilis, and there was no family history of tuberculosis. Enlargement of glands was first noticed in October, 1907, and subsided rapidly under treatment. The enlargement returned at Christmas, and at admission to hospital the mastoid, sub-maxillary, upper and lower cervical, axillary, and inguinal glands were all more or less enlarged, firm, discrete, and the skin over them healthy. Except for weakness, there were no other symptoms on admission. On February 17th profuse epistaxis occurred, followed by bronchitis, and later by pleurisy and diffuse broncho-pneumonia, with persistent fever, ranging from 100° to 103° F. Spleen slightly enlarged ; marked diminution in size of enlarged glands during the week before his death on March 18th. The sputum, on several examinations, contained no tubercle bacilli, and Calmette's reaction was negative.

The *post-mortem* examination was made on the afternoon of the day of death. The body was emaciated. The post-auricular, sub-maxillary, superior and inferior cervical glands, some of those in the posterior triangles, and the axillary, thoracic, and inguinal glands on both sides were enlarged, none to any great size ; they were discrete, pale on section, showed no yellow points or evidence of softening, and were firm. There was no pericarditis.

*Pleuræ.*—On both sides the visceral and parietal layers were universally and closely united by soft, recent adhesions. On the visceral layers were numerous small, round, white nodules, presenting a close resemblance to white tubercles.

*Lungs* (right, 25 oz. ; left, 32 oz.).—Both organs showed marked bronchitis ; the bronchial tubes contained an abundant muco-purulent secretion. On section the lower lobes of the lung were firm, deep red in colour, partly consolidated, but everywhere more or less crepitant. The cut surface was thickly sown with small glistening white nodules like those on the pleural surface. These were scattered over the whole lung, both upper and lower lobes. The left upper lobe showed the same congestion and areas of partial deep red consolidation as the lower; but the right upper lobe was less affected. The lobes were bound together by recent adhesions. The bronchial glands were slightly enlarged, but showed no other evidence of disease. A few enlarged mediastinal glands were noticed; they were pale in colour, and firm on section.

*Pericardium.*—Contained a slight excess of fluid.

*Heart* (weight, 9 oz.).—All the valves and the heart muscle were healthy.

*Liver* (weight, 67 oz.).—The capsule normal. The liver was in a state of marked congestion, and scattered over the cut surface there were many white or yellowish-white points about the size of a large pin's head, lying between the lobules.

*Gall-Bladder.*—Healthy.

*Spleen* (weight, 4½ oz.).—Somewhat enlarged. It was congested, soft in consistency, and on the cut surface were three or four pale, small areas like those in the liver. None of these nodules were visible under or in the capsule.

*Kidneys* (right, 8½ oz.; left, 8½ oz.).—Normal.

*Suprarenals.*—Healthy.

*Peritoneum.*—No ascites. On the peritoneum covering the third part of the duodenum were a few scattered pale nodules, of the same character as those of the pleura; none were found elsewhere, and the peritoneum was otherwise normal. The mesenteric glands were slightly enlarged, pale, and firm; they presented no yellow spots nor evidence of caseation or calcification.

*Intestines.*—Normal. No ulceration nor any other lesion was found anywhere in the intestinal tract.

*Brain.*—The brain and meninges were healthy in all respects.

Portions of the tissues were hardened in formalin, embedded in paraffin, and stained with hæmalum and eosin, Leishman's stain, carbol-fuchsin for tubercle bacilli, and Gram-Weigert for micro-organisms generally. After a careful search no tubercle bacilli or other micro-organisms could be found in any of the sections. For the differentiation of the varieties of the cell and general structure of the newly-formed tissue Leishman's stain gave the best pictures.

*Lymphatic Glands.*—Although much obscured and in parts greatly altered by the new elements, the different parts of the gland could in most cases be fairly well recognised. The capsule was not thickened, nor penetrated by growth, and there was no peri-adenitis. The cortical portion showed more of the normal structure than the medulla; both were greatly changed. The reticular framework of the gland was not markedly increased, and there was no such fibroid change as is seen in long-standing cases of lymphadenoma. The number of small lymphocytes was generally diminished. The cellular elements in the glands were made up of—

(1) Small lymphocytes varying in numbers,—in some parts scanty, in others about normal, in general deficient.

(2) Proliferated endothelial cells (presumably derived from the cells covering the retiform tissue, and lining the lymph sinuses,—these occurred in great abundance throughout the gland; with Leishman's stain the protoplasm was pink, relatively abundant; the nucleus central in position, small, round, staining a deep blue; sometimes two nuclei were present, in a few there were mitotic figures).

(3) Cells rather larger than (2); their protoplasm also staining pink, but with an excentrically placed and sometimes fragmented nucleus—presumably plasma cells. (In many parts these were very abundant, and in some occurred in groups, apparently actively proliferating, in the lymph sinuses.)

(4) Cells resembling a large lymphocyte of the blood, staining a pale blue throughout, with a large pale nucleus, clear nuclear network, protoplasm not abundant. (These occurred throughout, but chiefly in the medullary portion of the gland, and especially in parts which corresponded to the germ centres.) The cells apparently correspond to the mother cells of the germinal centres.

(5) Giant cells, the most striking of the cellular elements. These cells vary much in size and shape, from two or three times the diameter of a red blood cell to about eight to ten times this size. Both protoplasm and nuclei stained blue throughout. (The protoplasm stained uniformly, but sometimes contained dark blue granules. The nucleus stained deeply; when single, was large and rounded. There were in many cells two or three to four or more nuclei (one cell contained ten nuclei); large, oval or rounded, and generally situated in the body of the cell, and not at its periphery; the nucleoli were often conspicuous. Some of the cells contained large vacuoles. In others the nucleus or nuclei showed fragmentation. In some cells the nucleus was indented or reniform. These cells either occurred singly or in groups or rows in the lymph sinuses, and were numerous in the sinuses along the trabeculæ of the gland and under the capsule.)

Intermediate cells of all grades occurred between (4) and (5), and there were also cells resembling (4) in size, with a large oval nucleus, both nucleus and protoplasm staining a very dark blue, the nucleus being much the darkest. These cells and giant cells staining in a similar way were considered to be degenerating cells.

Lastly, these cells (4) and (5), with an occasional cell of group (2), were found in considerable numbers free in the lymph

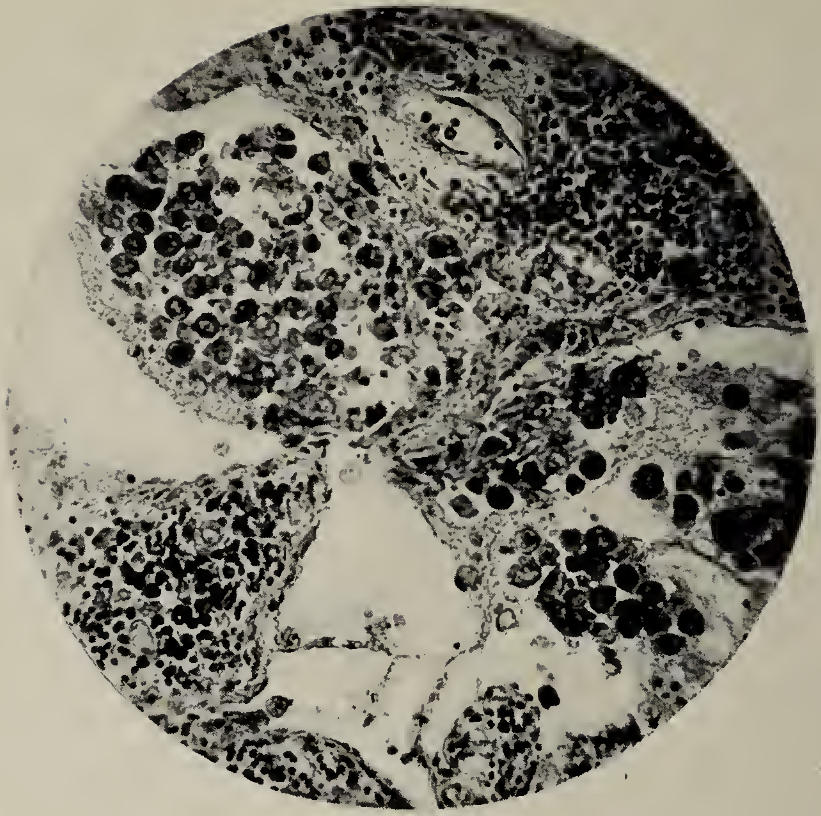


FIG. 1.

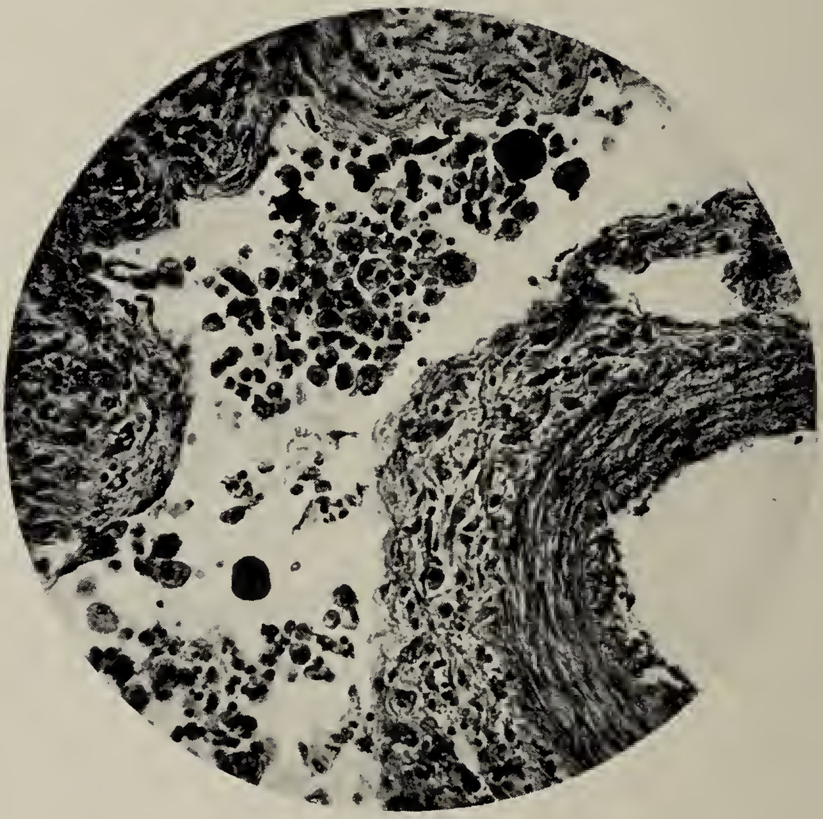


FIG. 2.

channels alongside the trabeculæ, where these were present, and under or in the gland capsule, and also in the large efferent lymph vessels at the hilus (Fig. 1). Long spindle or elongated cells, on the way to form connective-tissue cells, were present, but in very small numbers, as was to be expected from the acute character of the changes. The endothelial cells of small blood vessels appeared swollen in a few instances, but it was evident that these cells took little share in the cell proliferation. No eosinophile cells were seen anywhere.

*Lungs.*—The changes in the lungs were very extensive. First of all, there was throughout an intense bronchitis, affecting the larger and the secondary and tertiary bronchi. There were numerous small patches of broncho-pneumonia, with proliferating, desquamated endothelial cells in the alveoli, together with some fibrinous exudation in certain alveoli. The ordinary large pigmented cells of the lung were very abundant in alveoli, alveolar walls, and in peribronchial and perivascular lymph spaces. Capillary vessels showed a corresponding intense congestion, and all the above changes were acute in character. Nodules of lymphadenoma were very numerous, and were scattered throughout the lung, occurring most often in relation to the walls of bronchi, bronchioles, and alveolar passages. They were well demarcated from the lung, the older ones possessed an attempt at a capsule formed out of surrounding lung tissue, and in all cases they could be distinguished from broncho-pneumonic changes.

The nodules were composed of a fine reticular pink-staining stroma (Leishman), obscured by the very rich cellular contents. The cells were of the same character as those described in the lymph glands, and all kinds were represented. The pink staining cells of endothelial origin were present, not so numerous as in glands; they varied more in size, and many showed active mitosis. The other cells (4) and (5) stained blue, as in the glands. The giant cells were still larger and more conspicuous; some of them being enormous, and suggesting that they were irregular protoplasmic masses. Collections of these cells were seen in the subpleural veins, in the small veins of the lung itself (Fig. 2), and probably also in some lymphatics. The cells in the vessels were, as a rule, of type (4),—round or oval in shape, with a large, conspicuous nucleus, but numerous multinuclear giant cells were also seen, not so irregular in shape as in the tissues.

In the nodules under the pleura the cellular elements were less abundant, and there was a well-developed reticular framework, with many spindle cells, small and large; their nuclei were large, oval and round in shape; small lymphocytes were very few, giant cells comparatively few in number, but very conspicuous on account of their large size.

*Liver.*—The changes in the liver were interesting, as they appeared to show the stages in the formation of a lymphadenomous nodule. The smallest, and therefore presumably the earliest, foci consist of small aggregations of small lymphocytes, occurring between the acini of the liver, and not, so far as can be made out, in relation to any particular structure. Retiform tissue is either not visible or very scanty, possibly obscured by cells (Fig. 3). In the next stage, when the nodule is a little larger, the retiform (supporting) tissue is more marked, and in addition to the small lymphocytes, which are now fewer, there are present a few large cells (No. 4, above), staining blue throughout (Leishman), with generally one nucleus, occasionally two, the nucleus being large, round, or oval and centrally seated. In a larger nodule lymphocytes are very scanty, except at the periphery, when they are abundant. The nodule now mainly consists of a fine retiform tissue, with very abundant spindle or fibre cells, varying in size ; the other cellular elements are those described as present elsewhere, but are not abundant, the giant cells being few in number (Fig. 4). The liver capillaries show congestion around the nodule, and the liver cells perish from atrophy from pressure—no distinct capsule is formed, and the nodule appears to grow by an infiltration of the surrounding tissue by small lymphocytes.

*Spleen.*—The changes in this organ were not marked, the Malpighian bodies were large, and the lymphocytes in these appeared to be increased in number. Occasionally large lymphoid and giant cells were found in the splenic pulp,—and there were three or four small nodules of lymphadenoma. A hæmolymph gland examined was healthy.

I regret very much that the marrow of the long bones was not examined ; that of the ribs was not noticeably altered. The fact is, that although the clinical diagnosis made was lymphadenoma, when I saw the *post-mortem* appearances I thought this was a mistake, and that the case was an unusual one of tuberculosis, in spite of the absence of tubercle bacilli on repeated examination of the sputum. The nodules in the pleura, lung, and liver were macroscopically indistinguishable from tubercles. This, of course, is well known to occur, and is partly the reason why many cases of lymphadenoma have been assigned to tuberculosis. Histologically, the case is quite distinct from

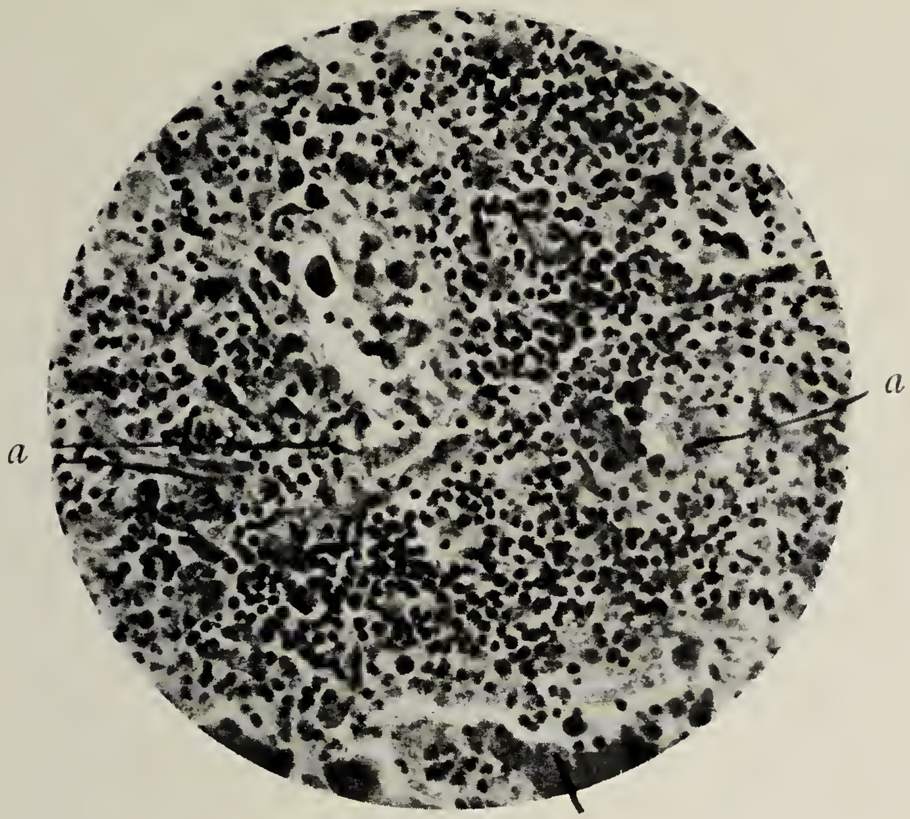


FIG. 3.

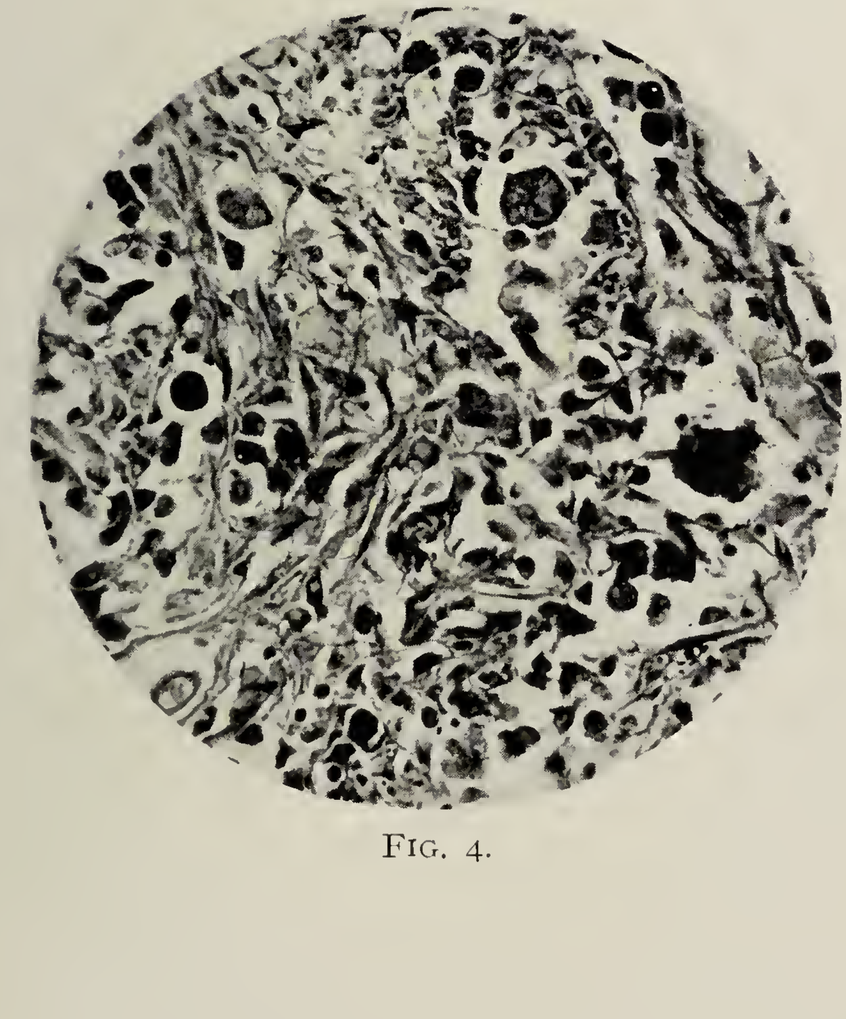


FIG. 4.

tubercle. I have described the lesions in some detail, as acute cases of lymphadenoma are rare, and afford a better opportunity of studying the structure of the newly-formed tissue than older cases in which there is more fibrosis. The lesions are typical of Hodgkin's disease or lymphadenoma as described by Andrews, Dorothy Reed, and others.

The liver showed best the way in which the new tissue is formed. The first stage of a lymphadenoma nodule is a collection of small lymphocytes, and the mode of spread in all stages appears to be by a lymphocytic invasion of the surrounding tissue at the periphery of the nodule. Next appears the formation of retiform tissue, together with cells resembling large lymphocytes, and then giant cells. Later still the structure becomes that of a retiform connective tissue together with the above cells, leading on to the condition seen in very chronic cases, where the patches become ultimately of fibroid character. The appearance in the first stage is indistinguishable from the earliest (miliary) collections of lymphocytes in lymphatic leukæmia, so far as regards the structure of the beginning minute nodules in both, but the latter disease is at once distinguished by the fact that in it the capillaries already contain lymphocytes in numbers.

The sections stained by Leishman's stain show that in the nodules in different organs the cells stain uniformly, and this enables one to differentiate them. In the glands the characteristic lymphadenoma cells or giant cells show all graduations in size, number of nuclei, etc., and stain similarly to the mother cells, or large lymphocytes in the germinal centres, which are greatly increased in numbers, and I believe the giant cells originate in this way from continual irritation or stimulation of these cells, by the cause of the disease, whatever that may be. The endothelial cells, which are also increased, have a different nucleus, and their protoplasm stains pink; they may also reach a considerable size and contain more than one nucleus, but when they do so their protoplasm still stains a uniform pink, and their nuclei are smaller and darker than those of the giant cells, and therefore I consider it improbable that the latter are derived from them, as has been stated. The absence of eosinophile cells, which could not be detected in any of the nodules by any of the stains employed, although they are usually present in the lesions of lymphadenoma, is possibly to be connected with the acute course of the illness; they have similarly been found absent in cases of acute leukæmia. The very extensive spread of the lesions in the lungs is a noticeable feature of the case. The passage of the cells into the veins is also remarkable; and this would probably occur more readily in the lungs than in other organs, on account of the large size and number of the capillary vessels.

The rapid diminution in size of the glands at the end of the illness was a noticeable feature.

The case shows that the lesion of true lymphadenoma or Hodgkin's disease, when seen in its acute form, is clearly of the nature of an inflammatory change with the formation of a peculiar granulation tissue. There is nothing here of the nature of a true hyperplasia of the lymphatic tissue, but rather a response on the part of the tissue to some continued irritation, the lesions approaching most nearly to those of the infective granulomata. They differ again from these, however, in the fact that the morbid changes which result from the irritation are limited to one particular tissue. It is this point which constitutes the peculiarity of lymphadenoma and separates it from other diseases. The affection of the lymphoid tissue varies in extent in different cases; it may be almost universally affected throughout the body, or more generally is confined to certain organs, the enlargement of the lymphatic glands being as a rule the first evidence of the disease. There seems no particular advantage in classifying cases according to the organs affected as has been proposed.

The disease has therefore nothing to do with a true hyperplasia of the lymphatic tissue, and it is on this account that I have avoided the use of the term pseudo-leukæmia, though neither lymphadenoma nor Hodgkin's disease are good names. The use of such a term as pseudo-leukæmia has been responsible for much confusion, and if the term is retained it would be an advantage to restrict it to the sense in which it has been employed by Sternberg (1905) for certain cases in which a true hyperplasia of the lymphoid tissue of the glands and internal organs occurs, but in which lymphocytes do not pass into the blood, as they do in lymphatic leukæmia, and are therefore not seen in the capillaries after death, as in the latter disease. Some of these cases, however, do end as lymphatic leukæmia, for Sternberg quotes undoubted examples by Paltauf, Pappenheim, and others in which a short time before death the passage of lymphocytes into the blood occurred. The process in true lymphadenoma or Hodgkin's disease is, however, essentially different, so that no such transformation into lymphatic leukæmia could occur, and cases in which a change has been alleged are probably cases of the lymphatic hyperplasia to which I have just alluded.

The question of the relation of the disease to tubercle is a more difficult one. Tuberculosis not unfrequently complicates lymphadenoma—so frequently that some authors, *e.g.* Benda, consider that the combination is not accidental, but that there is some etiological relationship between the two. In such cases the lesions of lymphadenoma occur side by side with those of tubercle, and according to Reed (1902) and others are distinct and can be readily distinguished—the one process going on independently of the other. There is a form of more or less generalised tuberculosis of the lymphatic system in which the changes, however, more closely resemble those of true lymphadenoma. In such cases in the glands and spleen large protoplasmic cells with one or more large deeply staining nuclei are described. In these cases, however, there are also in the glands and spleen areas of necrosis and of caseation, and the giant cells of tubercle, of different appearance from those of lymphadenoma, are generally found. In the spleen, if not also in the glands, distinct tubercles are to be seen, and in the large majority of cases tubercle bacilli can be demonstrated both in the glands and in the spleen. Further, in the tuberculous affection, in addition to areas of necrosis or caseation in the glands, there will be periadenitis and matting together of glands. Apart from the further proof by animal inoculations these histological appearances are sufficient to differentiate the cases. To the naked eye, however (as in this case in the lungs), the individual lesions of lymphadenoma may be indistinguishable from tubercles.

The newly-formed tissue of lymphadenoma with the peculiar large cells or giant cells which form the most striking characteristic of it, suggest some relation to tumours, and especially to sarcoma. One great point of difference is that in lymphadenoma the reaction or growth is confined to lymphoid tissue, and takes place only in that tissue ; other points against such a conception of lymphadenoma are well given by Sternberg (1905). They are that the growth does not pass beyond the gland or through the gland capsule, the character of the vessels, the condition of the ground substance and its relation to the cellular elements, the change from a tissue rich in cells to one poor in them occurs in different parts of the same section, and that the peculiar large cells occur only in parts more or less mingled with other tissue elements, and never form the tissue by themselves alone. Lastly, the growth tends ultimately to the formation of a fibroid tissue.

I am much indebted to Dr. E. V. Dunkley, pathologist to the hospital, for his help in investigating the case, and for excellent microscopic sections.

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## DESCRIPTION OF PLATE XI.

FIG. 1.—Lymphadenoma cells in large lymphatic vessels (? efferent) at hilum of gland.

FIG. 2.—Lymphadenoma cells of all sizes in vein of lung. There are several giant cells. The artery accompanying the vein is seen in the upper part of the picture.

FIG. 3.—Early stage of developing nodule of lymphadenoma in liver. At *a*, *a* remains of liver cells undergoing atrophy.

FIG. 4.—Late stage, or well-developed nodule in liver.

(Magnification of sections, about 300.)

## PRECAUTIONS TO BE OBSERVED IN ADMINISTRATION OF MILK IN DISEASE.

Before dealing very briefly with special diseases, a few general points about milk require to be borne in mind. Speaking generally, it is perhaps the most universally valuable nutriment in disease, and is most suitable wherever rapid growth or repair of tissue is taking place, as in children, young adults, and in convalescence from acute disease.

As compared with other proteid-containing foods, it calls out the smallest amount of secretion of gastric juice. The pancreatic juice secreted on a milk diet shows, however, a very high proteoclastic power ; hence the digestion of milk proteids takes place chiefly in the intestine, and the work of the stomach is spared. The proteid of milk is readily assimilated, and more completely used up than any other form. The proportion of fat is large, and in a state of emulsion, which is partly the reason why milk is especially valuable in wasting diseases and some nervous affections. Putrefactive processes in the intestines are reduced, as is also the quantity of uric acid excreted. On the other hand, some persons have such an invincible repugnance to or distaste for milk, that they find it impossible to take it.

On a pure milk diet, to obtain the requisite amount of calories a very large quantity of fluid must be taken. Three pints of milk, generally regarded as the minimum daily quantity, only contains sixty to seventy grammes of proteid, and this is not a sufficient amount for more than two or three weeks. To obtain the full amount of calories needful, five to six pints of milk must be taken daily. Besides the inconvenience of taking such a quantity of fluid, there is an excessive flow of urine, and in many persons uncomfortable peristaltic movements of the intestines. In the gastric digestion of milk, the dense and tough clots formed are often difficult of digestion, and cause epigastric discomfort or pain. Constipation is a well-known consequence of a milk diet in many persons. Two other drawbacks to milk are its low content of chlorides and of iron. From the former may arise disturbance in the osmotic processes of the body, and from the latter anæmia.

To turn to the drawbacks to the use of milk in gastric and intestinal affections. It must first be remembered that milk is not strictly speaking a fluid food, that it forms peculiarly dense masses of tough curd in the stomach, and that these are largely carried on into the intestines. Even when milk-digestion is well carried out—and in many persons this is a difficult matter—the fæces on a pure milk diet are bulky, and if large quantities are taken there is a probability that they will not all be properly dealt with, and that undigested curds will be passed in the fæces. In every case, therefore, in which a patient is on a pure milk diet the fæces should be frequently inspected.

In many cases of gastritis, or various forms of neurotic dyspepsia, a course of milk diet gives excellent results ; but in most it is advisable to add to the milk something to render the precipitated curds more flocculent, such as citrate of soda, lime-water or barley-water, or it may be peptonised. In cases of this class the important factor in the cure is that milk makes so little demand upon the gastric glands. In cases of gastric ulcer milk alone as the staple diet, even when one of the above adjuvants is added, is not so satisfactory. Recent observations have shown that it is difficult to maintain nutrition adequately on the reduced amount of milk that such patients can, as a rule, take without discomfort; consequently that the ulcer does not heal quickly, pain and other symptoms persist, and convalescence is protracted. Further, the large amount of fluid on a purely milk diet is disadvantageous by distending the stomach. A dietary containing more fat and proteid and less water, such as Lenhart's, conduces to a more speedy recovery; the nutrition is well maintained, the patients put on weight, and the protracted convalescence so often seen in cases of gastric ulcer treated for weeks on a pure milk diet is abolished. The fat in milk, being an emulsion, has probably no effect in reducing the excessive secretion of HCl generally present in ulcer.

Diseases of the stomach attended by dilatation, from whatever cause the pyloric obstruction may arise, are also not suitable for a pure milk diet, although they do well on small amounts of milk for a few days in beginning a course of treatment, because such stomachs are unable to dispose of the large quantity of fluid involved.

Similar objections apply to the use of milk alone in enteric fever. In the first place, something should always be added to the milk to render the curds more flocculent; and, econdly, it should be remembered that there is a more bulky residue in the intestines from milk than from many other forms of proteid-containing food. Then again it is impossible to adequately maintain the patient's nutrition on milk only through a long illness such as enteric fever. In enteric fever the milk curds may escape digestion, undergo putrefactive changes in the intestines, giving rise to excessive tympanites, or even to the absorption of toxic matters. Whenever there is much tympanites in enteric fever, the digestion of the milk used should be looked to, and it will often require to be peptonised. For many years I have given other articles of diet from the beginning of the illness in enteric fever, and I think that the patients have in consequence made a better and more speedy recovery, and had a less protracted convalescence. Whether they have shown less tendency to thrombosis of veins I cannot positively say. In convalescence milk can be given freely in addition to the other food, and is generally well digested.

In acute nephritis an absolute milk diet is undesirable because of (1) its high proteid content, and (2) the large amount of fluid involved to obtain a sufficient quantity of nutriment. Three pints of milk per diem is generally regarded as the minimum amount, and this contains sixty to seventy grammes of proteid, an insufficient quantity for the daily needs for more than two to three weeks, and too much water. Later, when the case has passed into a less acute stage, and the kidney begins to secrete water well, more milk can be given. Von Noorden, therefore, recommends the addition of cream in order to obtain the requisite number of calories from a smaller amount of milk. He also advises the addition of calcium carbonate to combine with the phosphoric acid of milk, which is badly excreted by the kidneys.

Albuminuria is not to be regarded as an indication for a pure milk diet. Albuminuria is in some cases a sign rather of past damage to the kidney than of actual and increasing mischief, and in such patients a mixed diet is best adapted to maintain their nutrition. In chronic parenchymatous nephritis, although some remarkable recoveries are recorded in which the patients lived for two years or more on milk only, the majority would neither tolerate such a diet nor do well upon it.

In contracted granular kidney the chief concern is to maintain the heart, and this is best done on a mixed diet. In most affections of the heart, and in diseases like pneumonia, which throw a heavy strain upon the circulatory mechanism, it is hardly necessary to say that a pure milk diet is unsuitable, because of the large amount of fluid that must be taken.

# ON THE COURSE OF PERNICIOUS ANÆMIA IN OLDER PERSONS.

In a disease like pernicious anæmia, which after all is not very common, it is difficult for one observer to get a sufficient number of examples from which to draw any general conclusions from his personal observations. Moreover, in hospital work, the opportunity to follow the course of a chronic disease for any considerable time is rare, especially in pernicious anæmia, as the course of the illness is characterised by marked exacerbations, during which the patient comes into hospital and is lost to sight during the intervals. To get a full knowledge of pernicious anæmia frequent observations on the blood are necessary throughout the course of the illness, including the remissions. The majority of cases of pernicious anæmia occur between the ages of 35 to 55 years, but for some time I had noticed in a few cases in elderly people that the disease appeared to follow a somewhat different course with especial features in the blood-changes, yet as they were not observed during long, continuous periods, it was possible that the variations observed might be only individual and accidental. Lately, however, I have had the opportunity of closely following the course of two cases in elderly men for about twelve months in each case, and in a third for six months.

In this paper I propose to deal with some features of pernicious anæmia where it occurs in elderly or old persons, of which I have eight cases available, and to compare them with cases occurring between the ages of 30 and 50, of which I have taken for comparison fifteen recent cases. The observations rest on a very large number of blood-counts, made or verified personally, and of which only the averages can be given in this paper. The hæmoglobin was estimated by Gowers's method or by Haldane's modification. Leishman's stain was used for films, supplemented by Jenner's stain when it seemed desirable. I do not propose to discuss at length what is and what is not true pernicious anæmia, other than to say that the evidence is in favour of its being a disease of the marrow brought about by the action of toxins varying in nature, the features of the disease being more or less constant and easily recognisable, due not to actual identity of the exciting cause in each case, but to the fact that the cause acts always primarily upon one and the same highly specialised tissue, the marrow, which responds in a constant way. The most important changes which give the disease its characteristic clinical features are of course found in the blood, and of these the high colour-index and the presence of macrocytes in large numbers seem to me the most important single changes, because the most constant, and because they are not regularly found in other forms of anæmia. To get their full significance, however, one or two blood-counts in a particular case are not sufficient, as occasionally the colour-index, especially in chronic cases, falls below 1. I am also of opinion that there is still something to be learnt as to the nature of pernicious anæmia from the variations in the number and variety of the leucocytes, and I have paid especial attention to this point.

The type of the disease in elderly persons, which conforms to what has been described as the chronic type of pernicious anæmia, though during the main part of its course it is of moderate severity, is not extremely protracted in duration; the etiology is as obscure and the onset as insidious as in other forms. In such persons most of the teeth have often been lost, and the remaining ones, especially the lower incisors, are loose with receding gums. In one case only the patient had had definite pus-formation, but this had been cured by extraction of the teeth and vaccines twelve months before the appearance of the distinctive anæmia. In three others without evidence of pus-formation cultures taken deeply from the root of the loosened teeth, after carefully cleansing the gums and superficial parts, only gave the presence of micro-organisms which Dr. Scott Williamson, pathologist to the hospital, considered were not pathogenic. Removal of the teeth had no effect on the course of the anæmia. In the other cases the teeth and gums were healthy, and this corresponds to my experience of pernicious anæmia generally—that the condition of the teeth is sometimes good, sometimes bad, but too variable to be of absolute significance in the origin of the disease. In several of the cases the patients were in easy circumstances, leading healthy lives under good hygienic conditions.

The duration in these cases is about twelve months, and the anæmia is definitely established by the time the patient seeks medical advice. At first there is not the great loss of strength which occurs early and is so marked a symptom in the more acute forms of pernicious anæmia, and for a long time the patient is able to get about and even to do a moderate amount of work without great fatigue and in fair comfort, except for some shortness of breath and palpitation. After a few months, however, loss of strength becomes marked, and then steadily increases until the fatal termination, which occurred in six of the eight cases; one I could not trace.

Although there are intervals in which the condition, both general and of the blood, improves, there are not the marked remissions which are so characteristic a feature of the more common type of pernicious anæmia; and on the whole with occasional intervals of improvement, the course of the disease is gradually but steadily progressive. Gastro-intestinal symptoms, which are so frequent in all forms of pernicious anæmia, so difficult to treat, and whose frequency and severity are of such great importance to the progress of the patient, are especially prominent in these cases, in the form of attacks of vomiting and diarrhœa, and especially of nausea, dryness of the mouth, and profound anorexia. This dryness of the mouth and anorexia are particularly difficult of relief. Probably, chiefly from these causes, there is a steady loss of flesh in the latter months of the illness, which becomes rapid towards the end. Beyond some tingling and numbness in feet and legs, signs of spinal affection were present in only one of these cases.

The patients show early and markedly the characteristic lemon-coloured tint of skin, and often a certain amount of scattered pigmentation. Hæmorrhages do not occur except in the form of retinal hæmorrhages, which were present in my cases. The spleen was not enlarged or very slightly so. In ordinary and more acute cases of pernicious anæmia I regard the presence of a well-marked urobilin band in the spectroscopic examination of the urine as a valuable confirmatory aid in the diagnosis, but in these more chronic cases it was only occasionally found. Towards the end of the illness the blood-pressure is apt to fall very low, possibly indicating exhaustion of the suprarenals. As to the condition of the blood in these eight cases the changes are of moderate severity, corresponding to those of the more chronic type of pernicious anæmia, and are given in the third line (*c*) of the Table II., p. 235, where it is seen that the red cells average about two millions, hæmoglobin 40 per cent., total leucocytes 5,720 per c.m., of which 35 per cent. are small lymphocytes and 9.5 large mononuclears. In line (*e*) two cases are given separately, as blood-counts were continuously taken at intervals of a fortnight during nine and twelve months respectively, and in (*d*) the six other cases, which were only seen for shorter periods. The condition of the blood in the prelethal stage (one week or so before death) is given separately for all these cases in line (*g*). The difference between (*c*), (*d*) and (*e*) illustrates what was said in the beginning as to the necessity of more continuous observations on the blood in cases of anæmia than we are able to secure in hospital practice where the patients come in for short periods when they are at their worst, and also in private practice, where ordinarily the blood is only examined occasionally at arbitrary intervals. It follows from this that (*d*), taken from patients discontinuously observed, gives too unfavourable a representation of the blood-state during the whole course of the illness, and that the average of red cells, hæmoglobin and leucocytes is seen to be higher when the cases continuously observed are taken into account.

The accompanying chart, Table I., brings out this point, and shows the course of the disease in the two cases continuously followed, an average being taken for each month. The chief points are that the red corpuscles and hæmoglobin follow corresponding curves and remain at a low, though not a very low, level during the whole course of the illness, and without any great remissions or variations until near the end, when they both show a rapid and steady fall until death occurred.

The curve of the small lymphocytes is also noteworthy, as it fairly closely follows that of the red cells and hæmoglobin, and temporary improvements in the case coincided with an increase in the percentage of small lymphocytes. I have noticed this also in myeloid leukæmia, improvement under different forms of treatment coinciding with an increase of these cells. Of course, it is to be borne in mind that in nearly all cases of pernicious anæmia there is a leucopenia, together with a relative increase

TABLE I.

| Case A. | Red Cells. | Hæmo-globin. | Colour-index. | Total Leucocytes. | Polymorpho-nuclears. | Small lymphocytes. | Large lymphocytes and mononuclears. | Eosinophils. |
|---|---|---|---|---|---|---|---|---|
|  | Per c.m. | % | % | Per c.m. | % | % | % | % |
| 1911. Sept. .. .. | 1,700,000 | 50 | 1.4 | 8,000 | 53 | 34 | 18 | 4 |
| Oct. .. .. | 2,100,000 | 50 | 1.2 | 7,600 | 72 | 16 | 10 | 2 |
| Nov. .. .. | 3,700,000 | 60 | .8 | 7,500 | 62 | 22 | 14 | 1 |
| Dec. .. .. | 3,100,000 | 60 | 1 | 10,000 | 59 | 29 | 7·4 | .6 |
| 1912. Jan. .. .. | 2,500,000 | 54 | 1.+ | 10,000 | 69 | 23 | 7 | ·3 |
| Feb. .. .. | 3,800,000 | 70 | 1.+ | 12,000 | 62 | 25 | 12 | .2 |
| March 5th .. | 2,400,000 | 45 | .9 | 4,500 | 49 | 39 | 11 | .2 |
| March 20th | 1,100,000 | 28 | 1.3 | 10,700 | 69 | 27 | 3 | 0 |
| Case B. |  |  |  |  |  |  |  |  |
| 1911. Nov. .. .. | 2,800,000 | 62 | 1.1 | 8,400 | 42·5 | 42 | 12 | 1·5 |
| Dec. .. .. | 3,000,000 | 70 | 1.1 | 7,000 | 39·5 | 45·5 | 15 | 1 |
| 1912. Jan. .. .. | 3,200,000 | 70 | 1 | 6,000 | 42 | 49 | 7·5 | 1 |
| Feb. .. .. | 3,700,000 | 70 | .9 | 6,000 | 51 | 35·5 | 10·5 | 1·5 |
| March.. .. | 3,100,000 | 68 | 1.1 | 11,500 | 39 | 38 | 19 | 3 |
| April .. .. | 2,200,000 | 60 | 1.3 | 5,000 | 36 | 44·5 | 17 | 1·5 |
| May .. .. | 2,900,000 | 60 | 1 | 4,300 | 37 | 43 | 16 | 2 |
| June .. .. | 2,800,000 | 62 | 1.1 | 9,000 | 64 | 20 | 14·5 | 2 |
| July .. .. | 3,400,000 | 55 | .8 | 9,200 | — | — | — | — |
| August .. | 1,300,000 | 28 | 1.1 | 6,500 | 65 | 18 | 12 | 2 |
| Sept. .. .. | 860,000 | 25 | 1.4 | 3,400 | 54 | 38 | 7·5 | 0 |
| Oct. 5th .. | 912,000 | 25 | 1.4 | 10,000 | 52 | 33 | 12 | 0 |

in the lymphocytes and mononuclears, expecially in the more chronic cases, and allowance must be made for this.

There are extraordinary variations in the total leucocytes for which I could not account, and which could not be accounted for by any variation in the clinical symptoms, nor do they correspond with the small variations in amounts or red cells and hæmoglobin. There is a marked rise of leucocytes in each case shortly before death. The polymorphonuclears show a remote correspondence with the variations in total number of leucocytes. Possibly these variations indicate an attempt on the part of the organism to react to the entrance of fresh doses of toxin.

Both these patients were treated at intervals with 10 to 20 c.c. doses of polyvalent antistreptococcic serum per rectum, but I could not trace out any effect from these injections on either the number or the percentage variety of the leucocytes.

To return to the eight cases taken together. The large mononuclears, though slightly increased in numbers, showed no striking variations. In these cases, however, these cells were generally of great size, and had large and very irregular nuclei, the nuclei having many lobes and often several vacuoles in them, the whole giving the impression that the cells were in a very active state. These are amœboid cells, and possibly show an attempted reaction on the part of the organism to infections or poisons with which the polymorphonuclears are unable to deal.

An important point about these cases in elderly persons is that both megaloblasts and normoblasts are either absent throughout the course of the disease until just before the end or present in very scanty numbers. This is true of chronic cases of pernicious anæmia generally, according to Gulland and Goodall, and is certainly a marked feature of the cases under consideration. This is one of the chief differences from pernicious anæmia in younger patients, or in the more ordinary acute or subacute forms, and might lead to an error of diagnosis if the presence of megaloblasts be taken as the criterion of the disease. Again, from the point of view of those who look upon pernicious anæmia as essentially a megaloblastic anæmia, this point might be considered sufficient to exclude these cases from the category. However, the fact that in the late stages there is an irruption of these cells into the blood, often in large numbers, thus bringing the condition of the peripheral blood into conformity with the general type, is a sufficient answer to this objection, for there could be no difference of opinion as to the films taken in the final stages presenting the blood-picture of megaloblastic pernicious anæmia. Macrocytes are numerous throughout, and my experience confirms the statement of Buckmaster, that of the abnormal changes in the blood this is the most constant in all forms of pernicious anæmia; I would add in association with a high colour-index.

Blood platelets are scanty in these cases. Chromatoplasia and granular degeneration of the red corpuscles, though generally present at intervals and towards the end, are not marked features. A few myelocytes, 1 per cent. or less, are found. In Table II. (*c*) is given the condition of the blood in these eight cases, and in (*a*) that of fifteen cases of pernicious anæmia below the age of fifty, several of them of acute type, based on an average of numerous blood-counts taken in all phases of the disease. It is seen that they differ in the following points.

In the former (*c*) the number of red cells is greater, percentage of hæmoglobin slightly higher, not so much in proportion as the number of red cells, and the colour-index lower, whilst the number of leucocytes is much greater, and the relative proportion of small lymphocytes and mononuclears is also higher. The contrast as regards leucocytes and lymphocytes would be even more marked but that the leucopenia happens in the fifteen cases in (*a*) to be less than the average usually given for ordinary cases of pernicious anæmia.

The contrast between the two types becomes far more striking, except as to one point, if the blood-state of the eight cases in (*c*) is compared with that in (*b*), which represents the average of a number of blood-counts from cases during the severe exacerbations which characterise the course of ordinary acute and subacute pernicious anæmia, and at the same time we remember that such severe exacerbations were absent in the eight older and more chronic cases (*c*). In the exacerbations the red cells and hæmoglobin, as compared with (*c*), are now reduced still further, to about half, the colour-index is correspondingly higher, and the leucopenia is very marked. On the other hand, there is one point in which the two conditions now approximate, and that is in the proportion of lymphocytes present, for these show a temporary but marked increase during exacerbations of the disease. In both (*a*) and (*b*), especially in the latter, the difference between them and (*c*) in the matter of megaloblasts and normoblasts is noteworthy.

The blood-state in severe exacerbations may be as bad as or worse than that seen in the prelethal stage of pernicious anæmia, *i.e.* within twenty-four to forty-eight hours of death, and it is interesting to note that patients may recover from such exacerbations and afterwards enjoy a long remission of comparatively good health, and that they often die with a condition of blood not so bad as it may have been in a previous exacerbation from which they made a good recovery.

I have had the opportunity of examining the blood in a number of cases of both the acute and chronic (or senile) type within twenty-four to forty-eight hours of death. The condition of the blood may then be taken to represent the

## TABLE II.

| | Red cells. | Hæmoglobin. | Index. | Total Leucocytes. | Polymorphonuclears. | Small lymphocytes. | Large lymphocytes and mononuclears. | Eosinophils. | Basophils. | Macrocytes. | Megaloblasts. | Normoblasts. | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | % | % | | % | % | % | % | % | | | | |
| (*a*) Blood from average of 15 cases under 50 years of age. | 1,575,000 | 36.8 | 1.2<br>—1.3 | 4,500 | 67 | 24 | 6.7 | .9 | .4 | numerous. | | | (*a*) |
| (*b*) The same during severe exacerbations. | 964,000 | 24 | 1.3 | 2,400 | 52.9 | 42 | 4 | .3 | .2 | numerous | about 20% | numerous. | (*b*) |
| (*c*) Blood from average of 8 cases over 55 years of age. | 2,120,000 | 40 | 1.0 | 5,720 | 53 | 35 | 9.5 | 2.4 | .4 | ,, | few or absent. | | (*c*) |
| (*d*) Blood from average of 6 cases in (*c*) over 55 years of age. | 1,754,000 | 35 | 1+ | 5,000 | 55 | 34 | 8 | 2.7 | .5 | ,, | absent or very few. | | (*d*) |
| (*e*) The same in 2 cases followed for last 12 months of life. | 2,680,000 | 48 | .9 | 7,800 | 60 | 29 | 9.4 | 1.4 | .2 | ,, | .3% | .2% | (*e*) |
| | 2,800,000 | 59 | 1.1 | 8,300 | 46 | 37.5 | 13.5 | 1.8 | .4 | ,, | absent. | .4% | |
| (*f*) The blood in prelethal state (within 48 hours of death) in cases under 50 years of age. | 850,000 | 17 | 1.8 | 2,400 | 54 | 35 | 10.2 | .2 | .2 | ,, | 10-40% | numerous. | (*f*) |
| (*g*) The same in prelethal states in cases over 55 years of age. | 1,000,000 | 25 | 1.3 | 9,700 | 55 | 31 | 12 | .3 | .4 | ,, | 12% | 3.5% | (*g*) |

ultimate result of the disease on the marrow. However great the differences in the blood between the two forms during the previous course of the disease, in the prelethal stage they closely approximate. The table (*f*) (*g*) gives the results in the two types. There is still a difference in severity, but now slighter as regards red cells, hæmoglobin and colour-index ; the chief difference is in the total leucocyte count, which rises towards death in the chronic or senile cases ; the relative numbers of the varieties of leucocytes closely approximate, the percentage of lymphocytes and mononuclears being high in both ; and there is now an irruption of megaloblasts and normoblasts into the blood in the chronic cases. This took place during the last two or three weeks of life in my cases and increased until death. Thus, as stated above, in the final stage of all forms of pernicious anæmia the blood-state is practically identical, and it follows that blood examinations made then would not show the differences found earlier.

Thus in the final stage of the type of case under consideration the blood-changes at last present the full picture of that of pernicious anæmia, with the difference that runs through the course of the case that there is no marked leucopenia and even a slight increase in the number of leucocytes. That this difference and the greater variations in the leucocyte count than occur in acute or subacute cases in younger patients may be due either to a different etiology or to a difference in reaction on the part of the marrow is obvious. There is no evidence to decide between these alternatives. Whatever the poison at work, it would seem to be combated rather by the lymphocytes and large mononuclears than by the polymorphonuclears.

A great deal can be done by treatment in mitigating the course and severity of the disease, though unfortunately the effects are not lasting. When the patient first comes under observation rest in bed is the first essential point, and next careful regulation of the diet with appropriate remedies for gastro-intestinal disturbances if these are present, as is generally the case. It must be seen that a sufficient amount of easily-digested food is taken, and the diet should include green vegetables and the juices of fruit. It need hardly be said that arsenic is the drug from which most benefit is derived, given not continuously but for definite periods, in gradually-increasing doses. In the type of case under consideration iron, preferably in the form of one of the so-called organic preparations, is certainly useful.

Several of the patients were treated from time to time with serum, and showed a marked improvement under it, in the earlier stages of the illness. This was manifested by an improved general sense of well-being and gain in strength, corresponding with amelioration in the state of the blood. As stated above, however, I could not connect any definite feature of the blood with the use of serum. It was not given in relation to the presence or absence of pyorrhœa. At first I used antistreptococcic polyvalent serum, later horse serum. It was given per rectum in doses of 10 to 15 c.c. daily for one to two weeks, then every other day for two to four weeks.

Two cases were treated by salvarsan; the one, a man, aged 62, showed a remarkable improvement. A mean of several counts, the blood before salvarsan, gave red cells 1,150,000, hæmoglobin 32 per cent., index 1.4, leucocytes 6,300, megaloblasts and monoblasts 2.4 per cent. Salvarsan was injected on July 6th. After steady improvement and gain of weight the counts gave on July 30th reds 4,200,000, hæmoglobin 65 per cent., index 8, leucocytes 10,700, no nucleated red cells. Unfortunately I have not been able to trace this patient, so that I cannot say whether he has remained well. In the other case there was little benefit.

# DISEASES OF THE LUNGS ASSOCIATED WITH THE PRESENCE OF FRIEDLÄNDER'S BACILLUS.

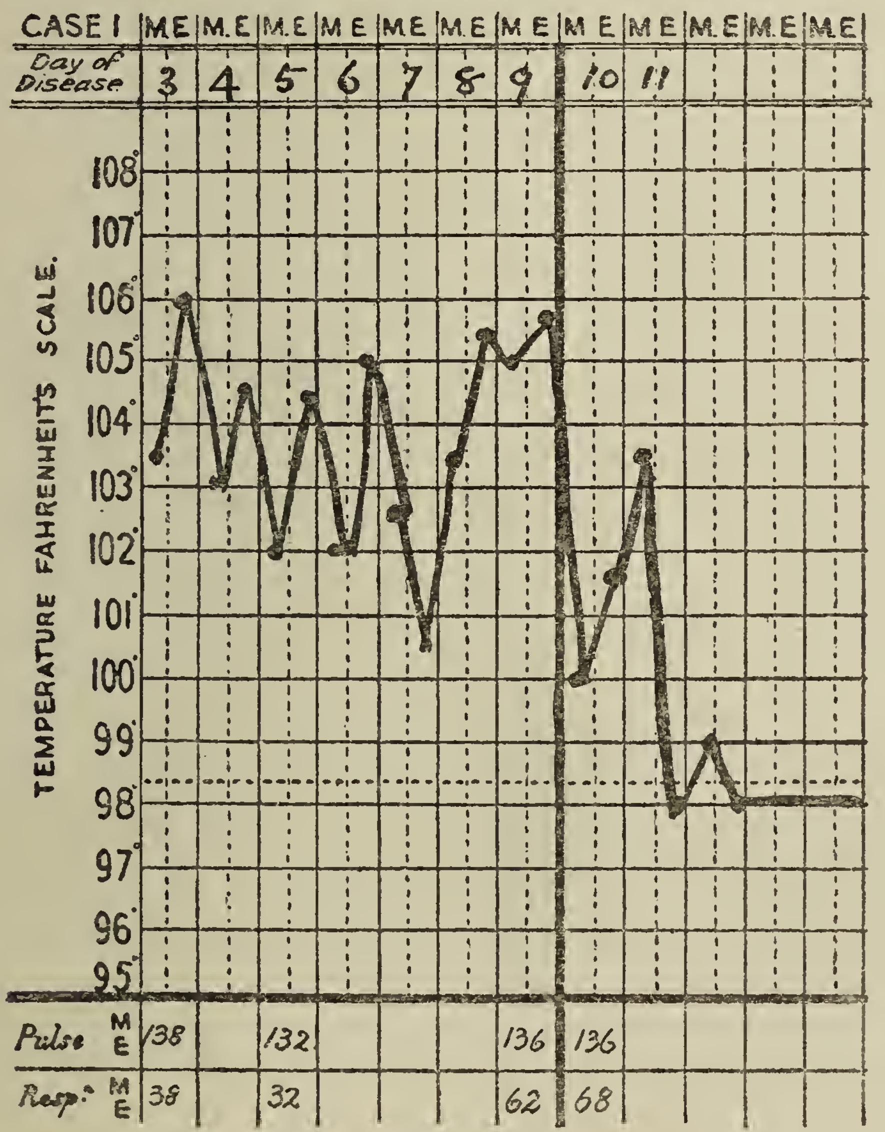
Several cases of pulmonary disease have recently been under my care in which Friedländer's bacillus was either obtained from the sputum in pure culture, or if in association with other organisms, appeared to be the chief morbific agent. The first question that arises is whether examination of the sputum can give an accurate representation of the process going on in the lung. Although there is considerable difference of opinion on this point, good authorities now hold that if the sputum is examined with certain precautions it does give such a representation. Bulloch[1] states that "in the careful and extended observations of Spengler there appeared to be a close connection between the conditions found in the sputum and lung respectively." In the following cases where there was a mixed infection that organism which was found ingested by the leucocytes was taken to be the important one.

B. Friedländer only accounts for a very small percentage of cases of pneumonia, and in these cases the lobar distribution is often due to an aggregation of lobular patches, with secondary patches of lobular pneumonia round the main area. The alveolar contents are viscid, due to a mucous secretion, the latter mechanically hinders the entrance of leucocytes into the alveoli, and therefore cells and fibrin are scanty.[2] The infiltration of the lung is apt to persist, and solution (lysis) of bacteria to be hindered because the bacilli are very resistant and cause only slight local reaction. Although it seems to be often a very severe affection, yet fever is often lower than in pneumococcal pneumonia, because on account of the slighter local reaction only few bacterial products are dissolved and absorbed. Abel and Hallwachs also state that there is a pronounced tendency to the formation of central patches of softening which may lead to the separation of necrosed patches of lung.

In mixed cultures B. Friedländer overcomes the pneumococcus.

It is well known that B. Friedländer is frequently present in affections of the nose and throat and elsewhere in the body, but in this paper I shall keep to pulmonary conditions. Friedländer's bacillus is found in pulmonary tuberculosis and chronic lung affections, in addition to being an occasional cause of pneumonia.

CASE I.—My first case was one of pneumonia of some severity, but of somewhat irregular course, in a girl aged 18, who had had no previous illness except enteric fever



five years before. The illness began acutely three days before admission to hospital with vomiting, pains in the right shoulder, a rigor, and high fever. She had eaten freely of ice cream the evening before the onset. On admission she was flushed, there was an outbreak of labial herpes, some diarrhœa, tongue thickly covered with a creamy white fur, pulse rate 140, respiration 38. Temperature 104°, rising to 106° the same evening.

Examination two days later showed dulness at the apex of the right lung, with bronchial breathing, coarse crepitations, and bronchophony; there were deficient resonance and air entry at the right base, with coarse moist crepitations. A few scattered finer râles were heard over the base of the left lung. For the first two days there was also some general bronchitis. The heart and abdominal organs were normal; the urine contained a trace of albumin. She coughed up a quantity of yellowish or yellowish green expectoration. Cultures made from this showed the presence of B. Friedländer and M. catarrhalis.

The illness ended by crisis on the eleventh day. The lung condition apparently cleared up completely, and she made a good recovery.

Differences from pneumococcal pneumonia are seen in the irregular oscillations of the temperature, the characters of the sputum, which was yellowish green, abundant and not blood-stained, and the absence, as shown by physical signs, of dense consolidation. Indeed, the signs at the right apex for two or three days suggested the possible formation of a cavity, and though the lung subsequently appeared to clear up, the case suggests, though it would not be safe to say more, that after such an illness the affected right apex might easily have contained a patch of necrosis, and become the starting-point of future disease, such as was found in Case 3.

In the next two cases the pulmonary lesions were those typical of chronic pulmonary tuberculosis with excavation. So typical were the lesions in character, and especially in distribution, that from the physical signs the diagnosis of chronic phthisis was confidently made, and when the pathologist reported that no tubercle bacilli could be found in the sputum after repeated and careful investigation, such a result was totally unexpected.

Case 2.—J. H., æt. 45, a labourer. No family history of consumption or other disease. He had never had syphilis. Three years ago he suffered from shortness of breath, with some cough and difficulty of breathing. No renal symptoms at that time. Two years ago he was in hospital for six weeks with cough, shortness of breath, and cramps in the legs. He completely recovered, lost his cough, and remained fairly well until two weeks before admission, when he was taken ill with a shivering fit, cough, shortness of breath, painful cramps in the limbs, and swelling of the legs and feet. He had had diarrhœa for some days.

September 12th, 1912. On admission he was pale, thin, and badly nourished. The temperature normal, pulse 84, of high tension, arteries thickened, respiration 20. Tongue foul, thickly furred. Legs and ankles swollen, and a "lumbar cushion" of œdema. Urine, sp. gr. 1010, contained a large amount of albumin, and numerous epithelial, hyaline and granular casts. Blood examination: red cells 4,700,000, whites 19,200 to c.m., hæmoglobin 86 per cent. Lungs: right upper lobe normal. At apex of left lung, front and back, there were dulness, bronchial breath-sounds, bronchophony, and some crepitations. At anterior part of axillary region was an area over which was dulness, cavernous breathing, bronchophony and pectoriloquy. At the lower angle of left scapula, over an area about three inches in diameter, were distinct signs of a cavity, *i.e.* high-pitched percussion note, cavernous breathing, liquid râles, post-tussive suction, and bronchophony. Coarse moist râles were heard over the bases of both lungs in front, and over the back of the chest as high as the lower angle of scapula. The heart was slightly enlarged, the blood pressure raised, and the edge of the liver felt about two inches below the ribs.

From the physical signs the condition of the lungs was looked upon as due to chronic tuberculosis with excavation. The sputum was large in quantity, purulent, and slightly offensive. The first culture showed presence of B. Friedländer and M. catarrhalis. Antiseptic inhalations were started from an oronasal inhaler, and carried out almost continuously. A second culture a week later gave a pure growth of B. Friedländer, and this continued to be the case whilst the patient was in hospital. Repeated examinations for T.B. were made, but always with a negative result. There were no elastic fibres in the sputum.

On October 1st a course of injections of a vaccine made from cultures of B. Friedländer was begun. At first five millions were injected, and the dose gradually increased up to five hundred millions. There was a slight local reaction at the site of injection after the first injection, but no reaction of any kind until the last dose was reached. One hour later the patient vomited, shivered, and the temperature rose to 101.8°. The result of treatment by rest, a full dietary, antiseptic inhalations, and specific vaccine was a gain in weight of 1½ stone, reduction of the large amount of purulent sputum to a negligible quantity, and no apparent effect on the kidneys except a slight fall in the amount of albumin in the urine ; in physical signs a striking diminution in the moist râles which on admission were so general over the lower part of both lungs, and with this relief of cough and shortness of breath ; no effect on the local lesions or cavities, which seemed to be steadily extending and involving fresh portions of lung at their margins. At left apex there were now " box-note " on percussion in front with liquid râles, bronchial breathing, and pectoriloquy. The physical signs at anterior part of left axilla and at lower angle of scapula remained much the same, but audible over a somewhat larger area. It is not possible to say what share in improvement is to be attributed to the vaccines. Although the man had gained weight and improved in some respects, his condition was far from satisfactory when he left the hospital, as the destructive process in the lung was still continuing. Friedländer's bacillus was still present when the sputum was last examined.

CASE 3.—A.B., æt. 31, cashier. Family history good. He had had two attacks of pneumonia, at the ages of 13 and 19. In the latter attack he was under my care, and on referring to the notes of his case I find that the pneumonia affected the whole of the right lung, and was most pronounced in the upper lobe ; that it was of somewhat irregular type, the temperature showing considerable oscillations, and coming down about the sixth day. The lung is stated to have cleared up satisfactorily. He had been in good health since then except for a cough at times. He attributed his present illness to chill. He was ill in bed for a fortnight before admission to hospital with severe pains in right side of chest, cough, large amount of expectoration, shortness of breath, heavy night-sweats, and for the first week his temperature ranged between 101° and 103°.

On admission his temperature was 101.5°, but fell to 99° the next day, and remained between 98° and 99° during the rest of the illness. Pulse 96, respiration 24. Tongue, thick yellow fur, urine normal. He looked thin and ill, there was no cyanosis. The chest was flat, narrow, and showed well-marked lateral groves.

Lungs: dulness over right apex, above clavicle and over first and second intercostal spaces in front and over suprascapular region behind, with bronchial breath-sounds, scattered moist râles, and bronchophony, and at outer anterior part of apex breath-sounds were cavernous, râles metallic, with post-tussive suction and pectoriloquy. On left side, at inner end of second intercostal space, in fifth and sixth space in axillary region, were patches of deficient resonance, with small moist crepitations. The breath-sounds were harsh, attended with rhonchi and a few coarse râles over the back of the right lung, as high as lower angle of scapula and over the extreme left base. The heart was normal. The sputum was copious, not offensive, in nummular masses. Repeated examinations for T. B. were negative. Cultures gave the presence of B. Friedländer. He stayed three weeks in the hospital, and made a steady and uneventful progress towards recovery under ordinary treatment. At the end of this time his cough was very slight, and there was practically no expectoration. He gained 5 lb. in weight during the last week of his stay, and felt quite well. The rhonchi and moist sounds had completely cleared up over both lungs, but there remained in the outer part of the right apex, towards the axilla, distinct signs of excavation in the presence of dulness, cavernous breath-sounds, post-tussive suction, and pectoriloquy.

The distribution and character of the lesions in these cases were thus exactly those of progressive pulmonary tuberculosis. This distribution of lesions, originating near the apex, and spreading downwards therefrom, with an early focus of disease in the apex of the lower lobe, is one of the most valuable and distinctive signs in the diagnosis of pulmonary tuberculosis. Further, this distribution of the lesions does not correspond to the ordinary position of bronchiectases, which usually most affect the lower lobes. In the first case, the history of indefinite chest illness well consorts with pulmonary tuberculosis, and the question arises as to the share played by B. Friedländer in the lung destruction. The man's resistance would have been lowered by the existing chronic Bright's disease, and we might suppose that the pulmonary lesions were indeed produced by the B. tuberculosis, and that subsequently the cavities were invaded by the B. Friedländer, which turned out the tubercle bacillus. If this supposition is correct, the patient's condition is no whit the better, for the work of destruction appeared to be actively going on. Such an explanation is more difficult in the second case, for the man was in good health until the onset of the present illness. In this case, however, it is difficult to suppose that a cavity apparently of some size could be produced in a fortnight. The previous history of two attacks of pneumonia is interesting, and also the known fact that the lung completely cleared up after the second attack. Bearing in mind the tendency of the B. Friedländer to cause local softening and necrosis, it is possible that the disease might have been insidiously going on for some time, until exposure to cold induced a sudden and considerable extension of mischief, and that the B. Friedländer might have been the only agent at work. If so, the close resemblance in physical signs to the lesions produced by B. tuberculosis is remarkable. On the whole, I incline to the view that in both cases the older lesions in the apices were produced by B. tuberculosis, and that a secondary infection by B. Friedländer occurred later, and caused the more general and patchy consolidation of the lungs. In both cases the onset of the present illness was marked by a very distinct sudden onset, with chills, fever, pains in the chest, and cough, with a very abundant purulent expectoration. In the subsequent course of the illness in each case, a notable fact is the maintenance of the temperature at or about normal, rarely exceeding 99°, in the presence of extensive excavation of the lungs, extensive areas of broncho-pneumonia, and the expectoration of large quantities of semi-purulent sputum. In the first case, the presence of chronic nephritis with its known tendency to cause a subnormal temperature, might partly account for the absence of hectic fever ; but in the second case there was no such source of explanation. The reason for the apyrexial course of the disease may be found in the general account of some of the characteristics of B. Friedländer given above.

In the other cases, B. Friedländer was found in association with other micro-organisms, and presumably had engrafted itself on pre-existing chronic pulmonary lesions. Thus in three cases there was fibrosis of the lung, in two accompanied also with bronchiectasis, the sequel of previous attacks of pneumonia. Of these cases, in one B. Friedländer was obtained in pure culture from the sputum, in another it was associated with a streptococcus, and in the third with M. catarrhalis. In all the sputum was large in quantity, thick, of a greenish yellow colour, and had a slight fœtor. In two of the cases a vaccine was used.

One patient was a single woman, aged 56. She had had nasal polypi removed, and for many years suffered from dyspepsia, but no other illness, and enjoyed fair health until four years ago, when she had left-sided pneumonia. Since then she had been in poor health, with loss of flesh, cough and expectoration daily of a quantity of muco-pus, which often had a disagreeable smell. She suffered from paroxysmal attacks of dyspnœa, in which she became extremely cyanosed. All symptoms had become aggravated since an attack of influenza six months previously. Examination of the chest showed on the left side thickening of pleura with fibrosis of the lung, and signs of bronchiectasis towards the base at the back, probably originating in an unresolved pneumonia. The heart's apex was displaced outwards from the contraction of the left chest. The other organs and the urine were normal. There was no œdema.

Examination of the sputum showed the presence of B. Friedländer and the pneumococcus. The lung was punctured, and from the material withdrawn the same organisms were cultivated. She was treated by rest, good feeding, intra-tracheal injections of izal and glycerine, and by a vaccine prepared from cultures of B. Friedländer, as Mr. Scott Williamson considered this to be the active organism. Injections, beginning with a dose of two millions, and increasing up to 500 millions, were given on July 9th, 10th, 11th, 12th, 13th, 20th, 23rd, 24th, 25th, 26th and 27th. The only direct effect noticed was that on two or three occasions there was a little redness and soreness of the arm at the site of injection. There was no change in the condition of the lung. A second mixed vaccine, of B. Friedländer and pneumococcus was then prepared, and five doses, ranging from 5 to 100 millions, were given between August 1st and 5th ; again without appreciable effect. She left the hospital on August 8th. The net result of six weeks' treatment was a considerable improvement in general health, a gain of 7 lb. in weight, great improvement in shortness of breath, and disappearance of the distressing attacks of dyspnœa, reduction of the large quantity of sputum to an inappreciable amount, and loss of fœtor of sputum and breath. The physical signs in the lungs remained practically unaltered.

Another of the cases was under the care of Dr. Symes, who has very kindly allowed me to use his notes.

The patient, a woman aged 24, was in hospital in August, 1912, with eclampsia, which was followed by double pneumonia. She was ill eight weeks. Since that time she had constantly coughed up large quantities of frothy greenish yellow sputum with an offensive odour. Repeated examinations for B. tuberculosis had given a negative result. Previous to this illness she enjoyed perfect health. Examination of the chest showed fibrosis of the lower lobe of the left lung with bronchiectases. Examination of the sputum showed presence of B. Friedländer and of M. catarrhalis. She was four weeks in hospital ; during the whole time the temperature was normal. A vaccine was prepared from cultures of B. Friedländer, and injected on July 14th, 16th, 18th, 21st, 23rd and 25th, beginning with a dose of five millions and increasing up to two hundred millions. No appreciable effect was observed on the temperature or otherwise from the injections. She gained 5 lb. in weight and improved in general health. The cough was much relieved, the quantity of sputum greatly reduced, and it became much less offensive. No note was made as to the condition of the lung, which was presumably unaltered as to the fibrosis and bronchiectasis.

The absence of any fever in both these cases is worthy of note.

In another case a man, whilst eating some chicken soup, swallowed one of the chicken's neck vertebræ; he felt it go "the wrong way;" and had a violent fit of choking and coughing, with subsequent pain in the upper part of the left chest. I saw him about eight months afterwards. He was then emaciated, weak, had a severe paroxysmal cough, and coughed up 8 to 12 oz. daily of yellowish offensive sputum. Examination showed deficient expansion, air entry, and resonance over the left lung, front and back, except the upper part of the upper lobe, over which the breath sounds were bronchial. Rhonchi were heard over the whole lung, with a few moist sounds at the extreme base. At the lower part of the left interscapular region, over an area of three inches in diameter, there was dulness, absent breath sounds at times, at others distant bronchial breathing, and increased vocal resonance. There was no fever, just as in the other cases. Friedländer's bacillus, pneumococci, and M. catarrhalis were found in the sputum. Mr. Scott Williamson considered the B. Friedländer to be the important organism, and although I was not very sanguine as to any good results whilst the bone was still there, I thought that a vaccine might possibly improve the condition of the surrounding lung. A course of vaccines was therefore given, but without result. The subsequent history is interesting. His wife came to visit him whilst she had acute influenza ; he contracted it from her, and the course of the illness entirely changed. For the next four weeks he had a swinging temperature of 100° a.m., to 102° or 103° p.m. Loud bronchial breathing and moist coarse crepitations appeared over the area of consolidation in the interscapular space. Examination of the sputum gave a pure culture of the B. influenzæ, which thus appeared to have turned out the other organisms. He insisted on going home, got gradually better, and one Sunday whilst in church he had a violent paroxysm of cough, and coughed up the chicken's vertebræ, which he brought up to show me.

I gratefully express my thanks to Mr. Scott Williamson for his careful bacteriological examinations in these cases.

## REFERENCES.

[1] Allbutt and Rolleston, *System of Medicine*, vol. v., p. 378.

[2] Abel and Hallwachs, *Handb. d. Pathogen., Mikro-organisms*, Jena, 1913, pp. 532-3.

# OBSERVATIONS ON TRENCH NEPHRITIS, ITS LATER STAGES AND TREATMENT.

THIS paper deals with cases of nephritis in a base hospital, the initial stage being over. All the patients came from France, except about six from Salonica, who showed no special features. The cases were taken in order of admission without selection. They were all under my immediate observation, and eighty cases seemed a sufficiently large number to represent the chief features of the disease.

The occurrence of nephritis on the large scale of the present war has afforded an opportunity of studying the first attack of the primary disease in young adults, which rarely occurs in civil hospitals, because in them the majority of cases of nephritis are exacerbations of a pre-existing disease. One would therefore be prepared for possible variations in the course and symptoms of the disease from those met with in civil practice, and possibly even for a new clinical type of nephritis, either as the result of the unprecedented physical conditions under which the men were placed and of a diet which mostly contained a relative excess of protein, or as the result of infection by a specific micro-organism. At the stage in which these cases were seen it seemed too late to make it worth while to carry out bacteriological investigations. The general result seems to point to a diffuse nephritis, chiefly affecting the convoluted tubules, [1] focal in distribution in the kidney, and presenting a corresponding clinical syndrome with some special but no absolutely distinctive features.

In view of the youth of most of the patients, it might be expected that some cases classed as nephritis would in reality turn out to be examples of " functional albuminuria " or " albuminuria of adolescents," but this was not the case, and, speaking generally, this form of albuminuria has hardly been seen at this hospital throughout the war.

Taking the 80 cases admitted to the hospital with the label " nephritis," there were only 6 in which the diagnosis was at fault, and in which the patient was suffering from some disease with secondary albuminuria.

The remaining 74, for convenience of reference, are placed in four groups :—

I. Thirteen cases in which there was either a distinct history of a previous attack of nephritis or definite signs of an affection of the kidneys of some standing.

II. Ten cases in which the nephritis was found to have cleared up on admission, though the symptoms of an attack before admission were quite definite.

III. Nineteen cases which completely recovered in hospital, and were discharged cured.

IV. Thirty-two cases which left this hospital not cured, though the majority were greatly improved.

## CAUSATION.

With regard to causation : In Group I., five, probably six, patients had had attacks of nephritis at some antecedent time, and one gave a family history of Bright's disease ; four patients had had scarlet fever severely, two recently, one diphtheria, followed by general anasarca, and four were either painters or plumbers before the war. In Group II., two had had scarlet fever, one recently, one trench fever shortly before, and one diphtheria three years before. In Group III., one had had scarlet fever, three bronchitis, and two malaria shortly before. In Group IV., three had scarlet fever in childhood, two diphtheria, four had recently suffered from malaria, but not severely, and in one the affection of the kidneys followed pneumonia eighteen months before. Twelve patients attributed the illness to standing in cold water, and four admitted alcoholism.

In three the illness began with a sharp attack of bronchitis, in two with pneumonia, in one with pleurisy and bronchitis, and in two with an attack of malaria. There was no case in which the nephritis came on directly after being "gassed," and very few of the patients had been "gassed" at any time.

## AGE.

The average age of the patients in Group I. was 31.8 years; in II. 24.9; in III., 27; and in IV., 31.7 years. Those in Groups II. and III., with early recovery, were thus decidedly younger than the others. Length of service appeared immaterial both to the incidence of disease and to its severity.

## ONSET.

The onset in nearly all appears to have been sudden, and œdema of the face and limbs, with pain in the back and dyspnœa the chief symptoms; the latter was only partly accounted for by the frequency of bronchitis. Œdema at onset was present in 57 out of 74 patients. Hæmaturia, generally slight, occurred in many.

## LATER SYMPTOMS.

The chief symptoms of the disease whilst in hospital were œdema, most often of the face and limbs, much less often general anasarca; as a general rule œdema showed a disposition to clear up fairly quickly, but in bad cases was, of course, persistent, sometimes for many weeks, and in a few attended with ascites and pleural effusion; dyspnœa, often but not always associated with some bronchial, or pulmonary complication; pains in the limbs and back, headache, less frequently vomiting, only occasionally diarrhœa, a feeling of great prostration, and sometimes mild cyanosis; anæmia was only present in the more severe cases and uræmic fits in one only.

### *Changes in the Cardio-Vascular Apparatus.*

The changes in the cardio-vascular apparatus are summarised in the table. The greater frequency of all cardio-vascular changes in Group I., where there was evidence of past kidney trouble, is to be noted, also that the blood pressure affords a fair index of the severity of the case. The pulse pressure seems a little large in all, and especially in the severe cases.

*Table showing Changes in Cardio-Vascular System.*

| | Hypertrophy of Left Ventricle. | Thickened Arteries. | Alteration in Heart Sounds. | Retinal Changes. | Average Blood Pressure in mm. Hg. | | |
|---|---|---|---|---|---|---|---|
| | | | | | Systolic. | Diastolic. | Pulse pressure. |
| Group I. (13 cases) | 5 | 5 | 11 | 5 | 147·9 | 90.8 | 57·1 |
| Group II. (10 cases) | 0 | 0 | 5 | 0 | 123 | 76 | 47 |
| Group III. (19 cases) | 0 | 0 | 9 | 2 (14) | 131 | 93·7 | 47·3 |
| Group IV. (32 cases) | 8 | 7 | 23 | 8 (29) | 143 | 91.2 | 52 |
| Total (74 cases) | 13 | 12 | 48 | 15 | | | |

In most cases several observations on blood pressure were made. The highest systolic taken was 198 mm. Hg. and the lowest diastolic 65 mm. Hg. The figures in brackets indicate the number of cases in which the particular symptom referred to was investigated. The blood pressure was taken in 10 cases in Group I.; in 6 cases in Group II.; in 13 cases in Group III.; and in 29 cases in Group IV.

The blood pressure was estimated by the auscultatory method with French's sphygmomanometer, and the diastolic pressure was taken as the point of disappearance of the loud third sound. The changes in the heart sounds consisted of a ringing or accentuated aortic second sound, with occasionally a systolic murmur or reduplicated first sound at the apex, and except in Group I. displacement of the apex-beat outwards, when present, was never great.

The retinal changes comprised two cases with intense retinitis, optic neuritis, numerous hæmorrhages and yellow-spot changes—both died; one of mild optic neuritis, who also died; three of mild œdema of the optic disc; two of pallor or œdema around the disc; and five of decided thickening of retinal arteries (one "silver wire" in a painter æt. 41). No other instance of retinal hæmorrhage was noted.

### *Urinary Changes.*

The quantity of urine was generally small for some days after admission; in severe cases 10 to 20 oz. a day. Later the quantity varied from 30 to 60 oz. a day, and was sometimes larger. Exceptionally the amount passed was small throughout, and some of these cases did quite well. Quite apart from treatment, there were periods of increased diuresis, as occurs in most forms of nephritis. An increased quantity of water did not always carry with it any considerable increase in the daily amount of urea.

The specific gravity of the urine was, generally speaking, low, the average being from 1015 to 1018, often below 1015, rarely over 1025, and fixation of specific gravity was seen in the more severe cases.

The quantity of albumin was often very large on admission, but in most soon diminished. In Group I. on admission the average amount in 9 cases was 0.89 per cent., and in 3 a trace, and on discharge in 4 a trace, in the rest 0.26 per cent.; in Group IV. the average quantity of albumin on admission in 22 cases was 0.46 per cent., in others a large to a small trace, and on discharge from 0.1 per cent. to a faint trace (Esbach's tubes).

Urinary casts were numerous on admission in most cases, except the mildest, and very abundant in the severe ones. They consisted generally of the epithelial, hyaline, and granular varieties, and fatty casts were rarely seen. In cases that recovered the casts rapidly diminished, but were very persistent in small numbers. These statements apply to centrifugalised urine.

Decided hæmaturia in hospital was exceptional; in many cases the urine was smoky on admission and for a short time afterwards, and this condition was apt to recur occasionally; in still more the only evidence of blood was microscopic.

With regard to the nitrogenous excretion, in 4 cases in Group I., several estimations in each, the nitrogen excreted as urea was 53 per cent. of the total nitrogenous intake; and in 10 cases in Groups III. and IV., several estimations in each, the average excretion was 67 per cent. of the intake. Urea was estimated by the hypobromite method, as more exact methods were not available. These cases may be taken as typical examples of varying degrees of severity.

As to excretion of NaCl, the amount in the food would vary from 4.5 to 6 grams a day; on the whole there was a deficiency in excretion of NaCl, but not to any great degree; it was most marked in severe cases and on admission, and improved as the case improved.

Thus in Group I. the average excretion of NaCl was 4.9 grams a day (average of 5 cases with several estimations in each), whilst in a fatal case it was only 3 grams a day, and in Group IV. the average excretion in 5 severe cases was nearly the same, 4.7 grams; and in 7 less severe cases it was 7.9 grams a day. In 3 of these it was at first as low as 1.5 to 2.2 grams.

Before estimations of urea and NaCl were made the patients had been on a fixed diet of known quantity for some days. Three teaspoonfuls of salt were given in water to two cases of average severity, and the excretion in the subsequent twenty-four hours was 10 and 12 grams respectively.

Phenol-sulpho-naphthalein tests were made on several occasions, and although in severe cases elimination was practically *nil,* unfortunately I can make no positive statement on this point, as the drug used was afterwards found by control tests to have deteriorated.

## Duration of Illness.

The average duration before admission to this hospital was two or three weeks, and that of the whole illness until the cases were sufficiently recovered for discharge was, in Group I. 9.6 weeks, in Group II. (convalescent on admission) three weeks, in Group III. (recovered in hospital) 6.8 weeks, and in Group IV. 8.1 weeks.

## Results.

The results were far worst in Group I.; of these 13 cases 1 died, 5 were discharged *in statu quo,* 5 showed some improvement, and in 2 only had the albumin and casts disappeared, and they might be considered well. Groups II. and III. are composed of cured cases. Of 30 cases in Group IV. 2 died, 3 were discharged not improved, 5 with casts and a considerable amount of albumin in the urine, and 12 with only a faint trace of albumin, or on some days none, and with a few casts present at intervals. The last 17 patients were sent to auxiliary hospitals, and subsequent inquiry has elicited that 5 have fully recovered, 6 are much better and doing light work, and 2 unchanged.

To sum up. Of 68 patients 3 died, 8 were discharged slightly improved as permanently unfit, 11 much improved but the urine contained casts and more than a trace of albumin, 6 fairly well and able to do light work, and 32 recovered completely; of 8 patients I have not sufficient information. It has already been pointed out that the younger patients gave the highest proportion of recoveries. It may also be noted that the only two cases in which there was intense retinitis and the only one with distinct optic neuritis died.

### *Ultimate Prognosis.*

I think that in those cases who left the hospital with urine free from albumin and casts, with a kidney functionating well, with a normal blood pressure and without signs of any cardio-vascular impairment, it is reasonable to expect a permanent cure, provided they are not placed under too unfavourable conditions. Probably the same may be said for those in whom the above conditions obtained, with the exception of a faint trace of albumin, and results of inquiry as to the subsequent condition of several of them support this view. If, as is probable, the nephritis is of focal distribution in the kidneys, persistence of a trace of albumin and a few casts in the urine may be attributed to the slow healing of a focal patch, the rest of the kidney being unimpaired, and the condition may be expected to clear up in time, though for this it is obviously essential that the patient should lead a careful life.

If there have been previous attacks of nephritis or evidence of pre-existing (to the attack) cardio-vascular-renal changes, then it is unlikely that the patient will completely recover.

With regard to cases in which, after a first attack, moderate or considerable albuminuria remains after three months, or there is evidence of cardio-vascular changes, further lapse of time is required to show the result, but the prognosis may be regarded as unfavourable, especially in men over thirty-five years of age.

## TREATMENT.

Rest in bed was insisted upon at first, and in all cases until either the albuminuria and casts had cleared up and there was a fair balance between the intake of nitrogenous foods and salt and the output by the kidney, or until it seemed that there was no prospect of the albumin and casts disappearing. The presence of blood in the urine was a further reason for complete rest, and also for great caution in increasing the amount of food, especially as to the addition of egg-yolk, fish, and chicken to the diet.

### *Diet.*

Severe cases were placed on milk only on admission. The large majority were on a fixed diet of milk 2½ pints, bread 6 oz., rice 1 oz., butter ½ oz., potatoes 4 oz., greens 4 oz., jam 1 oz., and fruit occasionally. As improvement took place the bread was increased to 8 oz. and the yolk of one or two eggs was added. Later on, 4 oz. of cooked fish or chicken were added and sometimes more bread and butter. Salt was not used as a condiment, nor added by the cook, except in cooking green vegetables. The amount of water was not restricted when once the kidney began to secrete freely. It is essential to know the amount of food by weight that a patient with nephritis is taking, and reliance cannot be placed on the ordinary hospital dietary unchecked, as the amount taken by individual patients varies greatly.

### *Drugs.*

Many of the patients had only a simple diaphoretic mixture with a saline or other purgative when required.

Hot-air baths were used when free diaphoresis was necessary. Nitroglycerin was given when the blood pressure was raised. Iron was given in the later stages if there was anæmia.

In many cases with deficient urinary excretion on admission, the treatment with sodium carbonate, suggested by Dr. Martin H. Fischer, was used with very satisfactory results in establishing a free flow of urine. Dr. Fischer attributes nephritis to an abnormal production and accumulation of acid in the kidneys and the œdema, anasarca, and other symptoms of nephritis to a similar process occurring in the tissues, and the object of his treatment is to diminish the concentration of acid by giving water freely and to neutralise it by an alkali. This may be given by mouth, or if not absorbed thus, by rectal or intravenous injection. The treatment is not suitable for chronic interstitial nephritis, which has a different origin.

Whatever view be taken of this explanation of the pathology of nephritis, there is no doubt that the treatment is often most efficient in producing free diuresis in about forty-eight to seventy-two hours with disappearance of œdema and relief of accompanying symptoms, such as dyspnœa, headache, etc.

Pure crystallised sodium carbonate ($Na_2CO_3 10 H_2O$) was given in doses of gr. x.–xv. in 8 oz. of water every hour during the daytime; the interval was increased to two to three hours after free diuresis had lasted two to three days. In two cases where administration per os was not feasible the rectal injections advised by Fischer (sod. carb. 10 grams, sod. chlor. 14 grams, water to 1 litre) were given every six to eight hours, but without success.

Most patients took this large quantity of fluid well, without special discomfort; two or three objected to it, and in three cases it had to be stopped because of nausea or vomiting. No other untoward effects were observed.

Reference can only be made to a few cases typical of many treated in this way. Charts 1 and 2 illustrate the rapid and free diuresis produced. Chart 3 shows a slower effect, the urinary excretion rising gradually with some fluctuation during four to five days and then maintaining a level of 80 to 110 oz. for eighteen days. The diuresis was followed by disappearance of œdema and amelioration of symptoms.

Chart 4 illustrates a very severe case in a patient, aged 20, with uræmic symptoms and extreme general anasarca. The effect of the alkaline treatment was remarkable; as the chart shows, in ten days the anasarca had disappeared, and from an apparently hopeless case he had become convalescent. In this case and in one or two others it has seemed to me that the combination of the alkaline treatment with digitalis and caffeine is efficient when they fail singly as diuretics.

Although the excretion of urea was also increased to a varying extent in different cases—for instance, in the

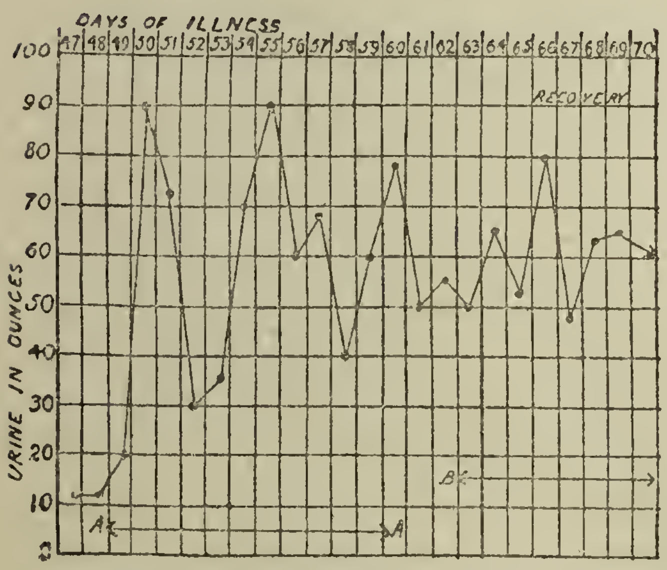


Chart 1.—Illustrating the rapid and free diuresis produced by administration of sodium carbonate (see also Chart 2). A–A, Sod. carb. gr. xv. hourly; bowels moved once daily. B, Trinitrin ♏ j of 1 per cent. solution four-hourly.

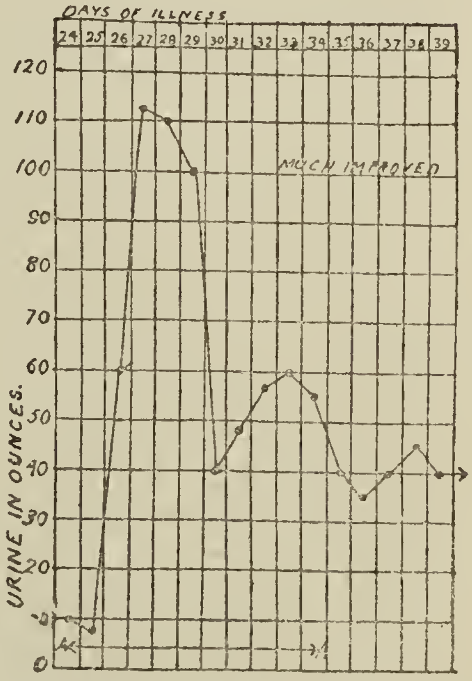


Chart 2.—From the 24th to the 29th day of illness sod. carb. gr. xij was administered every hour, and from the 29th to the 35th day every three hours. Bowels moved twice daily.

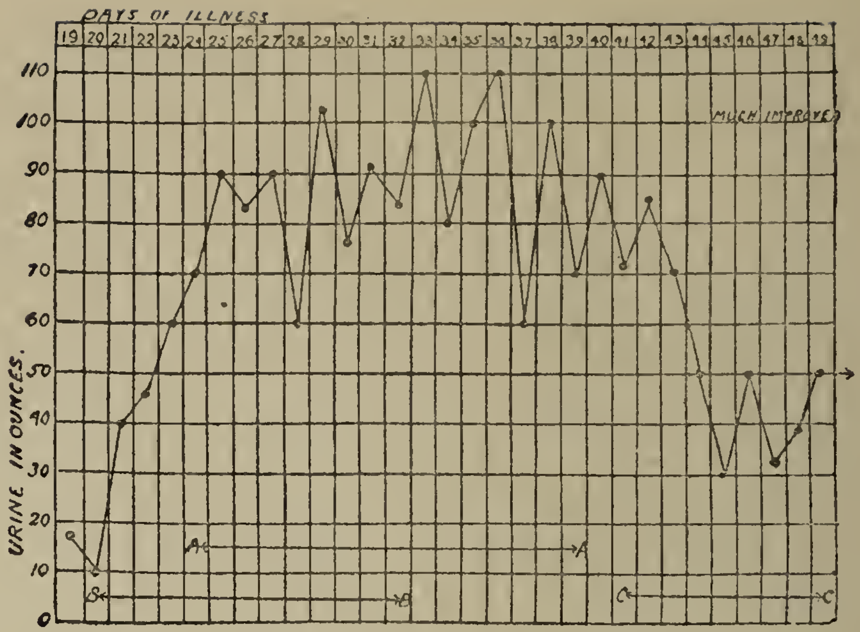


Chart 3.—Shows a slower effect of sodium carbonate. A–A, Adrenalin, 1 in 1,000, ♏ iij t.i.d. B–B, Sod. carb. gr. xv. hourly; bowels moved once daily. C–C, Tr. digitalis ♏ xx. twice daily. Patient had had scarlet fever twelve months before.

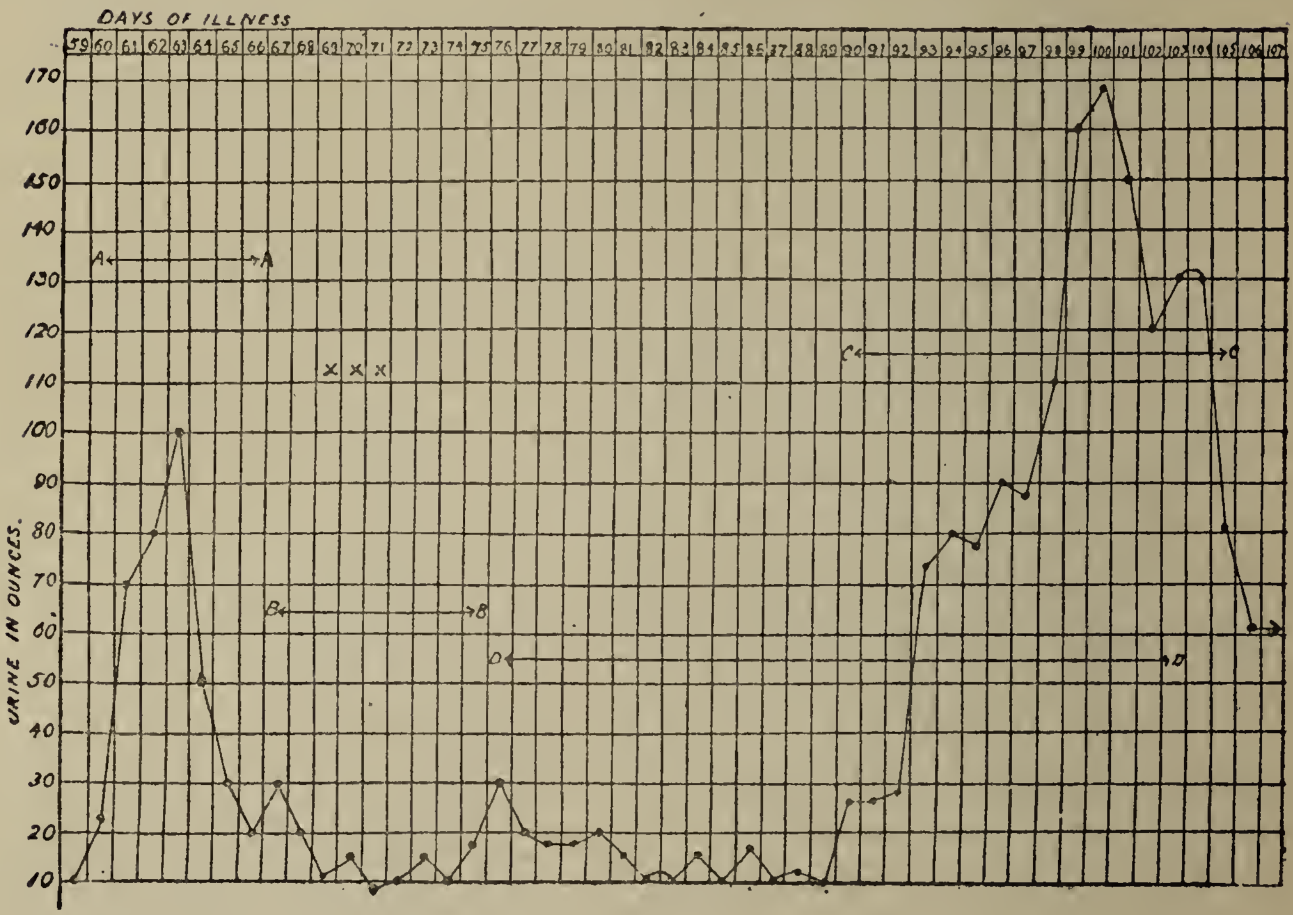


Chart 4.—A very severe case of trench nephritis. A–A, Sod. carb. gr. vij. hourly. ××× Saline enemata every six to eight hours on these days. B–B, Tr. digitalis ♏ xv. every six hours. C–C, Sod. carb. gr. xij. hourly from the ninetieth to the ninety-fifth day, every two hours for the remainder. D–D, Tr. digitalis ♏ xv., caffeine gr. v. every six to eight hours; twice daily after the 103rd day of illness; anasarca and dropsy disappeared.

foregoing case, on one day with 90 oz. urine, specific gravity 1010, urea excreted was 28.5 grams, or N 12.38 grams (with intake of N about 10 grams), albumin 12.75 grams, NaCl 28 grams—the chief effect was on the excretion of water and salts.

In a few cases the treatment failed for no ascertained reason.

In one case uræmic fits, the only instance in the whole series of cases, occurred on the sixth day of treatment, but they did not recur; free diuresis set in next day, dropsy disappeared gradually, and he made a good recovery.

### *Adrenalin.*

One other point in treatment may be mentioned. Several patients complained of feelings of great prostration, attended with a low blood pressure. Relief was given by the administration of adrenalin chloride (1 in 1,000) ♏iij to ♏v every four hours.

## PATHOLOGY.

With regard to the pathology I have little to say. Of the three fatal cases, a *post-mortem* was allowed in one only. This was a patient in Group IV., of 23 years of age, with no history of previous illness except bronchitis as a child. He had never had scarlet fever, nor been "gassed." He was admitted with œdema of the face and legs and general bronchitis, with coarse, moist râles over both lungs, slight enlargement of the left ventricle of the heart, and a systolic apex murmur. The systolic blood pressure was 198 mm. Hg, and the diastolic 140. Liver and spleen not enlarged. He had double optic neuritis and intense retinitis, with numerous hæmorrhages. The urine was scanty, specific gravity 1013 to 1016, contained a large quantity of albumin, no blood, and abundant hyaline, epithelial, granular, and fatty casts. He died of diffuse broncho-pneumonia, with some hæmoptysis. The sputum contained pneumococci.

The following is the report of the condition of the kidney:

> This shows a condition of focal nephritis with evidence of several acute attacks recent in date.
>
> Capsule thickened in patches. Blood vessels do not show arterio-sclerotic changes. Glomeruli normal in places; in others they show capsular fibrosis and fibrosis or atrophy of glomeruli; elsewhere there are intrascapular exudation, cell proliferation, and fibrosis. The interstitial tissue is increased in patches, and contains many areas of lymphatic spaces laden with fat.
>
> The convoluted tubules are almost normal here and there, but to a great extent show cellular degeneration, especially fatty desquamation and degradation of the lining cells and granular debris in the lumen. Some show dilation, and a few cystic spaces are present in the subcortical area.
>
> The heart shows interstitial myocarditis in some areas.
>
> The spleen, suprarenal, and pancreas are normal.

So far as this case goes it would confirm the clinical evidence, which points to this form of nephritis as being a diffuse nephritis, affecting chiefly the convoluted tubules, but not especially the vascular elements of the kidneys. The characters of the urine, with its rather low specific gravity, excretion scanty at first and later as a rule abundant, moderate or large amount of albumin, and with numerous hyaline, epithelial and granular casts in the early stages, correspond to a change of this kind.

To sum up. In cases of nephritis at a base hospital, the general clinical features perhaps especially characteristic are the benign character of the nephritis in the large majority, the frequency of pulmonary complications, especially bronchitis, œdema of lungs and broncho-pneumonia, apart from these complications a not infrequent dyspnœa, the generally good appetite, clean tongue, and maintenance of fair nutrition, and, on the other hand, infrequency of anæmia, of marked uræmic symptoms, and of a high blood pressure or cardio-vascular changes. The short duration of the illness in most cases would explain some of these latter departures from the usual symptoms of other types of nephritis. Severe retinitis or optic neuritis is uncommon—3 out of 80 cases.

I regret that more thorough investigations on the blood and on the excretion of uric acid, creatinin, etc., could not be carried out, and in conclusion it is my pleasing duty to thank the resident medical officers at Southmead Hospital, especially Captain H. H. Carleton, R.A.M.C., for much help in taking blood pressures and other investigations, and Professor Walker Hall, of the University of Bristol, for pathological reports, and to express our great indebtedness to the Medical Research Committee for their help in maintaining the pathological laboratory at Southmead Hospital, in which the urinary examinations were carried out.

## REFERENCE

[1] Davies and Weldon, *Lancet*, 1917, ii., 118.

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